disclosed are methods of preparing and using these antagonists.

TITLE: Method of inhibiting binding of PDGF to a PDGF receptor by biosynthetic PDGF antagonists
US PAT NO: 5,418,135 DATE ISSUED: May 23, 1995
:IMAGE AVAILABLE:
APPL-NO: 08/095,898 DATE FILED: Jul. 21, 1993
REL-US-DATA: Continuation of Ser. No. 632,068, Dec. 21, 1990, abandoned.

US PAT NO: 5,292,752 :IMAGE AVAILABLE: L1: 20 of 23
TITLE: Antithrombotic compounds

ABSTRACT:
The present invention is directed to a new class of piperidinyl medicinal agents which are useful as antithrombotic agents and as serotonin 5HT.sub.2 antagonists.

TITLE: Antithrombotic compounds
US PAT NO: 5,292,752 DATE ISSUED: Mar. 8, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/847,971 DATE FILED: Mar. 5, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 673,888, Mar. 22, 1991, abandoned, which is a continuation-in-part of Ser. No. 604,651, Nov. 1, 1990, abandoned, which is a continuation-in-part of Ser. No. 454,497, Dec. 21, 1989, abandoned.

APS/Medline
9/19/97

US PAT NO: 5,620,687 :IMAGE AVAILABLE: L1: 4 of 23
TITLE: Inhibition of intimal hyperplasia using antibodies to PDGF beta receptors

ABSTRACT:
Methods for inhibiting intimal hyperplasia in the vasculature of mammals, including primates, are disclosed. The methods comprise administering to the mammal an anti-PDGF receptor antibody, such as an anti-PDGF-alpha receptor antibody or an anti-PDGF-beta receptor antibody. The methods are useful in reducing intimal hyperplasia due to, for example, vascular injuries resulting from angioplasty, endarterectomy, reduction atherectomy or anastomosis of a vascular graft. The anti-PDGF receptor antibodies may optionally be administered coordinately with heparin, whereby the coordinately administered antibody and heparin are combinatorially effective in inhibiting intimal hyperplasia.

TITLE: Inhibition of intimal hyperplasia using antibodies to PDGF beta receptors
US PAT NO: 5,620,687 DATE ISSUED: Apr. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/366,860 DATE FILED: Dec. 30, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 304,623, Sep. 12, 1994, abandoned, which is a continuation of Ser. No. 23,504, Feb. 25, 1993, abandoned.

US PAT NO: 5,500,433 :IMAGE AVAILABLE: L1: 9 of 23
TITLE: Method of treating drug abuse

ABSTRACT:
The present invention is directed to a new class of piperidinyl medicinal agents which are useful for treating drug abuse.

TITLE: Method of treating drug abuse
US PAT NO: 5,500,433 DATE ISSUED: Mar. 19, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/371,063 DATE FILED: Jan. 10, 1995
REL-US-DATA: Continuation of Ser. No. 220,411, Mar. 30, 1994, abandoned, which is a continuation of Ser. No. 52,848, Apr. 26, 1993, abandoned, which is a continuation of Ser. No. 930,490, Aug. 14, 1992, abandoned, which is a continuation of Ser. No. 819,550, Jan. 10, 1992, abandoned, which is a division of Ser. No. 673,888, Mar. 22, 1991, abandoned, which is a continuation-in-part of Ser. No. 604,651, Nov. 1, 1990, abandoned, which is a continuation-in-part of Ser. No. 454,497, Dec. 21, 1989, abandoned.

US PAT NO: 5,418,135 :IMAGE AVAILABLE: L1: 16 of 23
TITLE: Method of inhibiting binding of PDGF to a PDGF receptor by biosynthetic PDGF antagonists

ABSTRACT:
Disclosed are polypeptides which antagonize the activity of platelet-derived growth factor (PDGF). These polypeptides include an amino acid sequence sufficiently duplicative of at least a portion of the amino acid sequence of an A chain of PDGF such that the polypeptides bind a cell membrane-bound receptor for native PDGF on a cell that responds biologically to the binding of PDGF. The binding of the antagonist to the receptor is effective to **inhibit PDGF** binding and activity. Also

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  *  such, of the data.                                                    *
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  *                  W E L C O M E   T O   T H E                         *
  *          U. S.   P A T E N T   T E X T   F I L E                     *
  * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

=> s platelet derived growth factor
         10851 PLATELET
        288984 DERIVED
        125926 GROWTH
        232109 FACTOR
L1        1105 PLATELET DERIVED GROWTH FACTOR
                 (PLATELET(W)DERIVED(W)GROWTH(W)FACTOR)

=> s (l1 or pdgf)(P)(antibody or antibodies)
           884 PDGF
         20317 ANTIBODY
         19286 ANTIBODIES
L2         220 (L1 OR PDGF)(P)(ANTIBODY OR ANTIBODIES)

=> s l2(p)(treatment or therapy or therapeutic or pharmaceutical)
        354494 TREATMENT
         33177 THERAPY
         48965 THERAPEUTIC
         68171 PHARMACEUTICAL
L3          63 L2(P)(TREATMENT OR THERAPY OR THERAPEUTIC OR PHARMACEUTICAL
)

=> s l3 and cell prolifera?
        190611 CELL
         14678 PROLIFERA?
          3449 CELL PROLIFERA?
                 (CELL(W)PROLIFERA?)
L4          36 L3 AND CELL PROLIFERA?

=> d kwic

US PAT NO:      5,662,904 :IMAGE AVAILABLE:                L4: 1 of 36

SUMMARY:

BSUM(22)

 The composition may also comprise active cytokines, for example
fibroblast growth factor or factors or other **cell** **proliferation**
or migration stimulating or glyco-aminoglycan stimulating factors in a
ra

=> d date 1-36

                                                            L4: 1 of 36
TITLE:          Anti-scarring compositions comprising growth factor
                  neutralizing antibodies
US PAT NO:      5,662,904                  DATE ISSUED:    Sep. 2, 1997
                :IMAGE AVAILABLE:
APPL-NO:        08/122,508                 DATE FILED:     Sep. 27, 1993
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FRN-PR. NO: 9106678
FRN-PR. CO: United Kingdom
PCT-NO: PCT/GB92/00570
FRN FILED: Mar. 28, 1991
PCT-FILED: Mar. 30, 1992
371-DATE: Sep. 27, 1993
102(E)-DATE: Sep. 27, 1993
PCT-PUB-NO: WO92/17206
PCT-PUB-DATE: Oct. 15, 1992

L4: 2 of 36

TITLE: Method and apparatus for treatment of focal disease in hollow tubular organs and other tissue lumens
US PAT NO: 5,662,609 DATE ISSUED: Sep. 2, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/226,945 DATE FILED: Apr. 13, 1994
REL-US-DATA: Continuation of Ser. No. 101,966, Aug. 4, 1993, Pat. No. 5,328,471, which is a continuation of Ser. No. 14,043, Feb. 5, 1993, abandoned, which is a continuation of Ser. No. 869,907, Apr. 15, 1992, abandoned, which is a continuation of Ser. No. 759,048, Sep. 5, 1991, abandoned, which is a continuation of Ser. No. 485,287, Feb. 26, 1990, abandoned.

L4: 3 of 36

TITLE: Methods of using enantiomerically pure hydroxylated xanthine compounds
US PAT NO: 5,652,243 DATE ISSUED: Jul. 29, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/343,810 DATE FILED: Nov. 22, 1994
REL-US-DATA: Division of Ser. No. 307,554, Sep. 16, 1994, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 4 of 36

TITLE: Enatiomerically pure hydroxylated xanthine compounds
US PAT NO: 5,648,357 DATE ISSUED: Jul. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/307,554 DATE FILED: Sep. 16, 1994
REL-US-DATA: Continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 5 of 36

TITLE: Method for purifying heregulin
US PAT NO: 5,641,869 DATE ISSUED: Jun. 24, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/456,201 DATE FILED: May 31, 1995
REL-US-DATA: Continuation of Ser. No. 126,145, Sep. 23, 1993, abandoned, which is a continuation of Ser. No. 880,917, May 11, 1992, abandoned, which is a continuation-in-part of Ser. No. 847,743, Mar. 6, 1992, Pat. No. 5,367,060, Nov. 22, 1994, which is a continuation-in-part of Ser. No. 790,801, Nov. 8, 1991, abandoned, which is a continuation-in-part of Ser. No. 765,212, Sep. 25, 1991, abandoned, which is a continuation-in-part of Ser. No. 705,256, May 24, 1991, abandoned.

L4: 6 of 36

TITLE: Substituted amino alcohol compounds
US PAT NO: 5,641,783 DATE ISSUED: Jun. 24, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/303,842 DATE FILED: Sep. 8, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 152,650, Nov. 12, 1993,

and Ser. No. 164,081, Dec. 8, 1993, Pat. No. 5,470,878.

L4: 7 of 36

TITLE: Polymeric endoluminal paving process
US PAT NO: 5,634,946 DATE ISSUED: Jun. 3, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/474,062 DATE FILED: Jun. 7, 1995
REL-US-DATA: Division of Ser. No. 118,978, Sep. 9, 1993, abandoned, which is a continuation-in-part of Ser. No. 987,357, Dec. 7, 1992, abandoned, which is a continuation of Ser. No. 857,700, Mar. 25, 1992, Pat. No. 5,213,580, which is a continuation of Ser. No. 593,302, Oct. 3, 1990, abandoned, which is a continuation of Ser. No. 235,998, Aug. 24, 1988, abandoned.

L4: 8 of 36

TITLE: Treatment of diseases using enantiomerically pure hydroxylated xanthine compounds
US PAT NO: 5,629,315 DATE ISSUED: May 13, 1997
:IMAGE AVAILABLE: DISCL-DATE: Jun. 1, 2015
APPL-NO: 08/456,900 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, abandoned, which is a division of Ser. No. 307,554, Sep. 16, 1994, abandoned, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 9 of 36

TITLE: Methods for treating disorders by administering radio frequency signals corresponding to growth factors
US PAT NO: 5,626,617 DATE ISSUED: May 6, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/575,840 DATE FILED: Dec. 20, 1995
REL-US-DATA: Continuation of Ser. No. 221,365, Mar. 31, 1994, abandoned.

L4: 10 of 36

TITLE: Process for preparing enantiomerically pure xanthine derivatives
US PAT NO: 5,621,102 DATE ISSUED: Apr. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/456,897 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, abandoned, which is a division of Ser. No. 307,554, Sep. 16, 1994, abandoned, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 11 of 36

TITLE: Enatiomerically pure hydroxylated xanthine compounds to treat inflammatory diseases
US PAT NO: 5,620,984 DATE ISSUED: Apr. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/456,898 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, which is a division of Ser. No. 307,554, Sep. 16, 1994, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a

continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 12 of 36

TITLE: Pyrido :2,3-D:pyrimidines for inhibiting protein tyrosine kinase mediated cellular proliferation
US PAT NO: 5,620,981 DATE ISSUED: Apr. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/433,294 DATE FILED: May 3, 1995

L4: 13 of 36

TITLE: Inhibition of intimal hyperplasia using antibodies to PDGF beta receptors
US PAT NO: 5,620,687 DATE ISSUED: Apr. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/366,860 DATE FILED: Dec. 30, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 304,623, Sep. 12, 1994, abandoned, which is a continuation of Ser. No. 23,504, Feb. 25, 1993, abandoned.

L4: 14 of 36

TITLE: Enantiomerically pure hydroxylated xanthine compounds to treat shock symptoms
US PAT NO: 5,612,349 DATE ISSUED: Mar. 18, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/457,062 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, abandoned, which is a division of Ser. No. 307,554, Sep. 16, 1994, abandoned, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 15 of 36

TITLE: Vascular endothelial growth factor-B and DNA coding therefor
US PAT NO: 5,607,918 DATE ISSUED: Mar. 4, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/469,427 DATE FILED: Jun. 6, 1995
REL-US-DATA: Continuation-in-part of Ser. No. 397,651, Mar. 1, 1995.

L4: 16 of 36

TITLE: Activation-state-specific phosphoprotein immunodetection
US PAT NO: 5,599,681 DATE ISSUED: Feb. 4, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/324,421 DATE FILED: Oct. 13, 1994
REL-US-DATA: Continuation of Ser. No. 918,370, Jul. 23, 1992, abandoned, which is a continuation-in-part of Ser. No. 866,728, Apr. 10, 1992, abandoned.

L4: 17 of 36

TITLE: Polynucleotides encoding connective tissue growth factor
US PAT NO: 5,585,270 DATE ISSUED: Dec. 17, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/386,680 DATE FILED: Feb. 10, 1995
REL-US-DATA: Division of Ser. No. 167,628, Dec. 14, 1993, Pat. No. 5,408,040, Apr. 18, 1995, which is a continuation of Ser. No. 752,427, Aug. 30, 1991, abandoned.

L4: 18 of 36

TITLE: Enatiomerically pure hydroxylated xanthine compounds
US PAT NO: 5,580,874 DATE ISSUED: Dec. 3, 1996

:IMAGE AVAILABLE:
APPL-NO: 08/457,68[redacted] DATE FILED: [redacted] Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, abandoned, which is a division of Ser. No. 307,554, Sep. 16, 1994, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 19 of 36

TITLE: Enatiomerically pure hydroxylated xanthine compounds to treat proliferative vascular diseases
US PAT NO: 5,580,873 DATE ISSUED: Dec. 3, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/456,899 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, which is a division of Ser. No. 307,554, Sep. 16, 1994, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 20 of 36

TITLE: Methods of determining chemicals that modulate transcriptionally expression of genes associated with cardiovascular disease
US PAT NO: 5,580,722 DATE ISSUED: Dec. 3, 1996
:IMAGE AVAILABLE:
APPL-NO: 07/832,905 DATE FILED: Feb. 7, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 555,196, Jul. 18, 1990, abandoned, which is a continuation-in-part of Ser. No. 382,712, Jul. 18, 1989, abandoned.

L4: 21 of 36

TITLE: Local polymeric gel therapy
US PAT NO: 5,575,815 DATE ISSUED: Nov. 19, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/132,745 DATE FILED: Oct. 6, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 118,978, Sep. 9, 1993, abandoned, which is a continuation-in-part of Ser. No. 987,357, Dec. 7, 1992, abandoned, which is a continuation of Ser. No. 857,700, Mar. 25, 1992, Pat. No. 5,213,580, which is a continuation of Ser. No. 593,302, Oct. 3, 1990, abandoned, which is a continuation of Ser. No. 235,998, Aug. 24, 1988, abandoned.

L4: 22 of 36

TITLE: R-enatiomerically pure hydroxylated xanthine compounds to treat baldness
US PAT NO: 5,567,704 DATE ISSUED: Oct. 22, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/457,683 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, which is a division of Ser. No. 307,554, Sep. 16, 1994, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 23 of 36

TITLE: Anti-proliferative effects of sodium butyrate
US PAT NO: 5,563,173 DATE ISSUED: Oct. 8, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/362,829 DATE FILED: Dec. 22, 1994

L4: 24 of 36

TITLE: Transgenic swine compositions and methods
US PAT NO: 5,523,226 DATE ISSUED: Jun. 4, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/063,095 DATE FILED: May 14, 1993

L4: 25 of 36

TITLE: Olefin substituted long chain compounds
US PAT NO: 5,521,315 DATE ISSUED: May 28, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/059,697 DATE FILED: May 10, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 3,372, Jan. 12, 1993, Pat. No. 5,354,756.

L4: 26 of 36

TITLE: Cell signaling inhibitors
US PAT NO: 5,470,878 DATE ISSUED: Nov. 28, 1995
:IMAGE AVAILABLE:
APPL-NO: 08/164,081 DATE FILED: Dec. 8, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 40,820, Mar. 31, 1993,
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=> d date 12-36

L4: 12 of 36

TITLE: Pyrido :2,3-D:pyrimidines for inhibiting protein tyrosine kinase mediated cellular proliferation
US PAT NO: 5,620,981 DATE ISSUED: Apr. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/433,294 DATE FILED: May 3, 1995

L4: 13 of 36

TITLE: Inhibition of intimal hyperplasia using antibodies to PDGF beta receptors
US PAT NO: 5,620,687 DATE ISSUED: Apr. 15, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/366,860 DATE FILED: Dec. 30, 1994
REL-US-DATA: Continuation-in-part of Ser. No. 304,623, Sep. 12, 1994, abandoned, which is a continuation of Ser. No. 23,504, Feb. 25, 1993, abandoned.

L4: 14 of 36

TITLE: Enantiomerically pure hydroxylated xanthine compounds to treat shock symptoms
US PAT NO: 5,612,349 DATE ISSUED: Mar. 18, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/457,062 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, abandoned, which is a division of Ser. No. 307,554, Sep. 16, 1994,

abandoned, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 15 of 36

TITLE: Vascular endothelial growth factor-B and DNA coding therefor
US PAT NO: 5,607,918 DATE ISSUED: Mar. 4, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/469,427 DATE FILED: Jun. 6, 1995
REL-US-DATA: Continuation-in-part of Ser. No. 397,651, Mar. 1, 1995.

L4: 16 of 36

TITLE: Activation-state-specific phosphoprotein immunodetection
US PAT NO: 5,599,681 DATE ISSUED: Feb. 4, 1997
:IMAGE AVAILABLE:
APPL-NO: 08/324,421 DATE FILED: Oct. 13, 1994
REL-US-DATA: Continuation of Ser. No. 918,370, Jul. 23, 1992, abandoned, which is a continuation-in-part of Ser. No. 866,728, Apr. 10, 1992, abandoned.

L4: 17 of 36

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US PAT NO: 5,585,270 DATE ISSUED: Dec. 17, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/386,680 DATE FILED: Feb. 10, 1995
REL-US-DATA: Division of Ser. No. 167,628, Dec. 14, 1993, Pat. No. 5,408,040, Apr. 18, 1995, which is a continuation of Ser. No. 752,427, Aug. 30, 1991, abandoned.

L4: 18 of 36

TITLE: Enatiomerically pure hydroxylated xanthine compounds
US PAT NO: 5,580,874 DATE ISSUED: Dec. 3, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/457,685 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, abandoned, which is a division of Ser. No. 307,554, Sep. 16, 1994, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 19 of 36

TITLE: Enatiomerically pure hydroxylated xanthine compounds to treat proliferative vascular diseases
US PAT NO: 5,580,873 DATE ISSUED: Dec. 3, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/456,899 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, which is a division of Ser. No. 307,554, Sep. 16, 1994, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 20 of 36

TITLE: Methods of determining chemicals that modulate transcriptionally expression of genes associated with cardiovascular disease

US PAT NO: 5,580,722 DATE ISSUED: Dec. 3, 1996
:IMAGE AVAILABLE:
APPL-NO: 07/832,905 DATE FILED: Feb. 7, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 555,196, Jul. 18, 1990, abandoned, which is a continuation-in-part of Ser. No. 382,712, Jul. 18, 1989, abandoned.

L4: 21 of 36

TITLE: Local polymeric gel therapy
US PAT NO: 5,575,815 DATE ISSUED: Nov. 19, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/132,745 DATE FILED: Oct. 6, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 118,978, Sep. 9, 1993, abandoned, which is a continuation-in-part of Ser. No. 987,357, Dec. 7, 1992, abandoned, which is a continuation of Ser. No. 857,700, Mar. 25, 1992, Pat. No. 5,213,580, which is a continuation of Ser. No. 593,302, Oct. 3, 1990, abandoned, which is a continuation of Ser. No. 235,998, Aug. 24, 1988, abandoned.

L4: 22 of 36

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US PAT NO: 5,567,704 DATE ISSUED: Oct. 22, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/457,683 DATE FILED: Jun. 1, 1995
REL-US-DATA: Division of Ser. No. 343,810, Nov. 22, 1994, which is a division of Ser. No. 307,554, Sep. 16, 1994, which is a continuation of Ser. No. 13,977, Feb. 4, 1993, abandoned, which is a continuation-in-part of Ser. No. 926,665, Aug. 7, 1992, abandoned, which is a continuation-in-part of Ser. No. 846,354, Mar. 4, 1992, abandoned.

L4: 23 of 36

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US PAT NO: 5,563,173 DATE ISSUED: Oct. 8, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/362,829 DATE FILED: Dec. 22, 1994

L4: 24 of 36

TITLE: Transgenic swine compositions and methods
US PAT NO: 5,523,226 DATE ISSUED: Jun. 4, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/063,095 DATE FILED: May 14, 1993

L4: 25 of 36

TITLE: Olefin substituted long chain compounds
US PAT NO: 5,521,315 DATE ISSUED: May 28, 1996
:IMAGE AVAILABLE:
APPL-NO: 08/059,697 DATE FILED: May 10, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 3,372, Jan. 12, 1993, Pat. No. 5,354,756.

L4: 26 of 36

TITLE: Cell signaling inhibitors
US PAT NO: 5,470,878 DATE ISSUED: Nov. 28, 1995
:IMAGE AVAILABLE:
APPL-NO: 08/164,081 DATE FILED: Dec. 8, 1993
REL-US-DATA: Continuation-in-part of Ser. No. 40,820, Mar. 31, 1993, abandoned.

L4: 27 of 36

TITLE: Acetal or ketal substituted xanthine compounds
US PAT NO: 5,440,041 DATE ISSUED: Aug. 8, 1995
:IMAGE AVAILABLE:
APPL-NO: 08/194,135 DATE FILED: Feb. 8, 1994
REL-US-DATA: Continuation of Ser. No. 4,353, Jan. 14, 1993, abandoned.

L4: 28 of 36

TITLE: Connective tissue growth factor(CTGF)
US PAT NO: 5,408,040 DATE ISSUED: Apr. 18, 1995
:IMAGE AVAILABLE:
APPL-NO: 08/167,628 DATE FILED: Dec. 14, 1993
REL-US-DATA: Continuation of Ser. No. 752,427, Aug. 30, 1991, abandoned.

L4: 29 of 36

TITLE: Structure, production and use of heregulin
US PAT NO: 5,367,060 DATE ISSUED: Nov. 22, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/847,743 DATE FILED: Mar. 6, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 790,801, Nov. 8, 1991, abandoned, which is a continuation-in-part of Ser. No. 765,212, Sep. 25, 1991, abandoned, which is a continuation-in-part of Ser. No. 705,256, May 24, 1991, abandoned.

L4: 30 of 36

TITLE: Olefin-substituted long chain xanthine compounds
US PAT NO: 5,354,756 DATE ISSUED: Oct. 11, 1994
:IMAGE AVAILABLE:
APPL-NO: 08/003,372 DATE FILED: Jan. 12, 1993

L4: 31 of 36

TITLE: Smooth muscle mitogen
US PAT NO: 5,328,986 DATE ISSUED: Jul. 12, 1994
:IMAGE AVAILABLE: DISCL-DATE: Jul. 20, 2010
APPL-NO: 07/832,845 DATE FILED: Feb. 10, 1992
REL-US-DATA: Continuation-in-part of Ser. No. 766,354, Sep. 26, 1991, abandoned, which is a continuation-in-part of Ser. No. 604,778, Oct. 26, 1990, Pat. No. 5,229,493.

L4: 32 of 36

TITLE: Method and apparatus for treatment of focal disease in hollow tubular organs and other tissue lumens
US PAT NO: 5,328,471 DATE ISSUED: Jul. 12, 1994
:IMAGE AVAILABLE:
APPL-NO: 08/101,966 DATE FILED: Aug. 4, 1993
REL-US-DATA: Continuation of Ser. No. 14,043, Feb. 5, 1993, abandoned, which is a continuation of Ser. No. 869,907, Apr. 15, 1992, abandoned, which is a continuation of Ser. No. 759,048, Sep. 5, 1991, abandoned, which is a continuation of Ser. No. 485,287, Feb. 26, 1990, abandoned.

L4: 33 of 36

TITLE: Methods and compositions; purified preparation of neural progenitor regulatory factor
US PAT NO: 5,276,145 DATE ISSUED: Jan. 4, 1994
:IMAGE AVAILABLE:
APPL-NO: 07/852,755 DATE FILED: Mar. 17, 1992
REL-US-DATA: Continuation of Ser. No. 389,841, Aug. 4, 1989, abandoned.

L4: 34 of 36

TITLE: Smooth muscle mitogen
US PAT NO: 5,229,493 DATE ISSUED: Jul. 20, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/604,778 DATE FILED: Oct. 26, 1990

L4: 35 of 36

TITLE: DNA sequences encoding bVEGF120 and hVEGF121 and methods for the production of bovine and human vascular endothelial cell growth factors, bVEGF.sub.120 and hVEGF.sub.121
US PAT NO: 5,219,739 DATE ISSUED: Jun. 15, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/559,041 DATE FILED: Jul. 27, 1990
REL-US-DATA: Continuation-in-part of Ser. No. 450,883, Dec. 14, 1989, which is a continuation-in-part of Ser. No. 387,545, Jul. 27, 1989, abandoned.

L4: 36 of 36

TITLE: Production of vascular endothelial cell growth factor
US PAT NO: 5,194,596 DATE ISSUED: Mar. 16, 1993
:IMAGE AVAILABLE:
APPL-NO: 07/450,883 DATE FILED: Dec. 14, 1989
REL-US-DATA: Continuation-in-part of Ser. No. 387,545, Jul. 27, 1989, abandoned.

=> d kwic 32

US PAT NO: 5,328,471 :IMAGE AVAILABLE: L4: 32 of 36

ABSTRACT:
Diseased . . .
prior to the introduction of the therapeutic agent. Then, the diseased region is treated with a therapeutic agent to suppress **cell** **proliferation** in the diseased region. The plaque is then disrupted. Finally, the occluded region may be treated with a medicament to. . .

SUMMARY:

BSUM(5)

In . . . of violation of the intimal barrier may be stimulated by platelets and macrophages in the blood, leading to smooth muscle **cell** **proliferation** and a regeneration of the stenosis. Disease conditions, such as advanced ulcerated atherosclerotic lesions, and in some instances intervention techniques,. . .

SUMMARY:

BSUM(20)

A . . . prior to the introduction of the therapeutic agent. Then, the diseased region is treated with a therapeutic agent to suppress **cell** **proliferation** in the diseased region. The plaque is then disrupted, for example by conventional balloon angioplasty, atherectomy, laser plaque removal or. . . PTCA failure. Thus, the anti-proliferative therapy will further reduce the likelihood of long term restenosis, through inhibition of smooth muscle **cell** **proliferation** which is maximum during the first 12 to 24 hours following treatment.

DETDESC:

DETD(2)

As used in the specification and claims of this application, the term "**therapeutic** agent" refers to substances which alter the metabolism of the cells or reduce the tendency for thrombosis within the diseased. . . agents i.e. colchicine and alkylating agents; intercalating agents; growth modulating factors such as interleukins, transformation growth factor b, congeners of **platelet** **derived** **growth** **factor** and monoclonal **antibodies** directed against growth factors; anti-thrombotic agents, e.g., anti-GIIb/3a, trigramin, prostacyclin and salicylates; thrombolytic agents e.g. streptokinase, urokinase, tissue plasminogen activator. . . healing response to vessel or organ injury post intervention. Anti-proliferative drugs or high efficacy anti-inflammatory drugs are also useful for **treatment** of focal vasculitides or other inflammatory arteritidies, e.g., granulomatous arteritis, polyarteritis nodosa, temporal arteritis and Wegner's granulomatosis. Anti-inflammatory agents are. . . help heal dissections, flaps and aneurysms. Exemplary adhesives include cyanoacrylates, gelatin/resorcinal/formol, mussel adhesive protein and autologous fibrinogen adhesive. The term "**therapeutic** agents" does not encompass solubilizing or dissolving agents which disrupt the atherosclerotic plaque.

```
=> d his

     (FILE 'USPAT' ENTERED AT 09:01:05 ON 19 SEP 1997)
L1          1105 S PLATELET DERIVED GROWTH FACTOR
L2           220 S (L1 OR PDGF)(P)(ANTIBODY OR ANTIBODIES)
L3            63 S L2(P)(TREATMENT OR THERAPY OR THERAPEUTIC OR PHARMACEUTI
CAL
L4            36 S L3 AND CELL PROLIFERA?

=> logoff y
U.S. Patent & Trademark Office LOGOFF AT 09:12:04 ON 19 SEP 1997


 ********
Welcome to DIALOG

Dialog level 97.08.03D

Last logoff:  04aug97 15:01:56
Logon file405 19sep97 08:15:43
ANNOUNCEMENT   ****    ANNOUNCEMENT   ****    ANNOUNCEMENT

? b 155

       19sep97 08:16:11 User217743 Session D414.2
            $0.00    0.004 Hrs File410
     $0.00  Estimated cost File410
     $0.00  Estimated cost this search
     $0.00  Estimated total session cost   0.007 Hrs.

File 155:MEDLINE(R)  1966-1997/Nov W2
       (c) format only 1997 Knight-Ridder Info

      Set  Items  Description
      ---  -----  -----------
? s pdgf and (antibodies or antibody) and cell()prolif?

           4151  PDGF
         316183  ANTIBODIES
         315260  ANTIBODY
        1142543  CELL
         120676  PROLIF?
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          28483  CELL(W)PROLIF?
      S1    115  PDGF A[redacted] (ANTIBODIES OR ANTIBODY) [redacted]D CELL()PROLIF?
? s s1 and py>1991

            115  S1
        2132219  PY>1991
      S2     73  S1 AND PY>1991
? s s1 not s2

            115  S1
             73  S2
      S3     42  S1 NOT S2
? s s3 not py=1991

             42  S3
         375769  PY=1991
      S4     28  S3 NOT PY=1991
? t s4/6/all


 4/6/1
07040819   91069052
  Tyrosine kinase and control of %%%cell%%% %%%proliferation%%%.


 4/6/2
07029258   90153981
  Heparin-binding growth factor-1 stimulation of human endothelial cells
induces platelet-derived growth factor A-chain gene expression.


 4/6/3
06650489   90253811
  Coexpression of the genes for platelet-derived growth factor and its
receptor in human T-cell lines infected with HTLV-I.


 4/6/4
06510598   91046141
  The biology of mesangial cells in glomerulonephritis.


 4/6/5
06320443   88127122
    Mitogenesis in response to %%%PDGF%%% and bombesin abolished by
microinjection of %%%antibody%%% to PIP2.


 4/6/6
06256466   89023579
   Mesangial cells express %%%PDGF%%% mRNAs and proliferate in response to
%%%PDGF%%%.


 4/6/7
06255550   89008866
    Expression of platelet-derived growth factor (%%%PDGF%%% )-related
transcripts and synthesis of biologically active %%%PDGF%%%-like proteins
by human malignant epithelial cell lines.


 4/6/8
06248396   88242725
```

Human arterial smo[redacted] muscle cells in [redacted]lture. Effects of platelet-derived growth factor and heparin on growth in vitro.

4/6/9
06246805 88217341
Identification and purification of %%%PDGF%%%/sis-like proteins from nuclei of simian sarcoma virus-transformed fibroblasts.

4/6/10
06237889 88087290
Platelet-derived growth factor receptors expressed by cDNA transfection couple to a diverse group of cellular responses associated with %%%cell%%% %%%proliferation%%%.

4/6/11
06181314 85231534
Production of %%%PDGF%%%-like growth factors by embryonal carcinoma cells and binding of %%%PDGF%%% to their endoderm-like differentiated cells.

4/6/12
05964679 88177982
Expression of platelet-derived growth factor receptors is induced on connective tissue cells during chronic synovial inflammation.

4/6/13
05942907 87010390
Ionic signalling by growth factor receptors.

4/6/14
05930773 86079499
A significant part of macrophage-derived growth factor consists of at least two forms of %%%PDGF%%%.

4/6/15
05900024 90126368
%%%PDGF%%% receptors on cells of the oligodendrocyte-type-2 astrocyte (O-2A) cell lineage.

4/6/16
05897714 90078634
Activation of cultured rat hepatic lipocytes by Kupffer cell conditioned medium. Direct enhancement of matrix synthesis and stimulation of %%%cell%%% %%%proliferation%%% via induction of platelet-derived growth factor receptors.

4/6/17
05891378 89372566
Regulation of c-fos messenger ribonucleic acid by fibroblast growth factor in cultured Sertoli cells.

4/6/18
05878028 89081988
Prognostic significance of mRNA-encoding estrogen receptor and epithelial

growth factor receptor in breast carcinoma progression into lymph nodes: 1. Estrogen receptor encoding mRNA.

4/6/19
05803829 89391820
Immune mechanisms in atherosclerosis.

4/6/20
05678879 89170980
Interleukin-1 promotes proliferation of vascular smooth muscle cells in coordination with %%%PDGF%%% or a monocyte derived growth factor.

4/6/21
05566690 88245966
Induction of B-type receptors for platelet-derived growth factor in vascular inflammation: possible implications for development of vascular proliferative lesions.

4/6/22
05374308 88196247
Classification system based on the functional equivalency of mitogens that regulate WI-38 %%%cell%%% %%%proliferation%%%.

4/6/23
05310429 87211843
Platelet-derived growth factor.

4/6/24
05299249 87114209
Platelet-derived growth factor as a mediator of normal and neoplastic %%%cell%%% %%%proliferation%%%.

4/6/25
05269101 86122955
The role of platelets in the development and complications of atherosclerosis.

4/6/26
05255830 87304570
Effects of epidermal growth factor and platelet-derived growth factor on c-fos and c-myc mRNA levels in normal human fibroblasts.

4/6/27
05006999 87079876
Calcium in the action of growth factors.

4/6/28
04691010 85218798
Microinjected c-myc as a competence factor.
? t s4/3,ab/5,24,25

4/3,AB/5

DIALOG(R)File 155:MEDLINE(R)
(c) format only 1997 Knight-Ridder Info. All rts. reserv.

06320443 88127122
Mitogenesis in response to %%%PDGF%%% and bombesin abolished by microinjection of %%%antibody%%% to PIP2.
Matuoka K; Fukami K; Nakanishi O; Kawai S; Takenawa T
Department of Pharmacology, Tokyo Metropolitan Institute of Gerontology, Japan.
Science (UNITED STATES) Feb 5 1988, 239 (4840) p640-3, ISSN 0036-8075 Journal Code: UJ7
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The turnover of phosphatidylinositol 4,5-bisphosphate (PIP2) is believed to constitute a crucial step in the signaling pathways for stimulation of cells by a variety of bioactive substances, including mitogens, but decisive evidence for the idea has not been obtained. In the present study, a monoclonal %%%antibody%%% to PIP2 was microinjected into the cytoplasm of NIH 3T3 cells before or after exposure to mitogens. The %%%antibody%%% completely abolished nuclear labeling with [3H]thymidine induced by platelet-derived growth factor and bombesin, but not by fibroblast growth factor, epidermal growth factor, insulin, or serum. The findings strongly suggest that PIP2 breakdown is crucial in the elicitation and sustaining of %%%cell%%% %%%proliferation%%% induced by some types of mitogens such as platelet-derived growth factor and bombesin.

4/3,AB/24
DIALOG(R)File 155:MEDLINE(R)
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05299249 87114209
Platelet-derived growth factor as a mediator of normal and neoplastic %%%cell%%% %%%proliferation%%%.
Westermark B; Heldin CH
Med Oncol Tumor Pharmacother (ENGLAND) 1986, 3 (3-4) p177-83, ISSN 0736-0118 Journal Code: LSP
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW
Human platelet-derived growth factor is the major mitogen in serum for connective-tissue-derived cells in culture. The factor is 30,000 mol. wt protein composed of two disulphide-linked polypeptide chains, named A and B. The B-chain is virtually identical to part of the transforming protein of simian sarcoma virus (SSV), implying that SSV-transformation is mediated by a %%%PDGF%%%-like growth factor. This notion is supported by the finding that specific as well as nonspecific inhibitors of %%%PDGF%%%-action (%%%PDGF%%% %%%antibodies%%% and suramin, respectively) are efficient inhibitors of SSV-transformation and revert the transformed phenotype of SSV-transformed cells. Expression of the genes encoding the %%%PDGF%%% subunits and production of %%%PDGF%%% -like growth factors is a common feature of human sarcoma cell lines, suggesting a role of %%%PDGF%%% in the pathogenesis of sarcomas, although direct support in favor of this notion is lacking. An involvement of %%%PDGF%%% in autocrine and paracrine stimulation of normal cell growth is suggested by the finding that responsive (arterial smooth muscle cells and placental cytotrophoblasts) as well as nonresponsive (endothelial cells and macrophages) cells produce %%%PDGF%%%-like growth factors. In conclusion, %%%PDGF%%% -like growth factors may be widely implicated in normal as well as neoplastic growth processes.

4/3,AB/25
DIALOG(R)File 155:MEDLINE(R)

05269101 86122955
The role of platelets in the development and complications of atherosclerosis.
Packham MA; Mustard JF
Semin Hematol (UNITED STATES) Jan 1986, 23 (1) p8-26, ISSN 0037-1963
Journal Code: UN9
Languages: ENGLISH
Document type: JOURNAL ARTICLE; REVIEW

Although lipids have received most attention in relation to atherosclerosis, vessel injury also has a role in the development of atherosclerotic lesions. Thrombi that form at sites of injury can be incorporated into the wall, causing thickening, and platelets that adhere to damaged vessel walls release a growth factor (%%%PDGF%%%) that stimulates smooth muscle %%%cell%%% %%%proliferation%%%. The early lesions of atherosclerosis are focal and develop around vessel orifices and branches in relation to the patterns of blood flow and areas of increased permeability and endothelial cell damage. Platelets also contribute to the complications of advanced atherosclerosis caused by occlusive thrombi, thromboembolism, and spasm. The causes of vessel wall injury are not established, although there is evidence pointing to disturbed blood flow, hypertension, antigen--%%%antibody%%% complexes, complement, materials originating from platelets and white blood cells, bacteria, endotoxin, viruses, smoking, dietary lipids, homocystinemia, diabetes, other metabolic disorders, and stress. Platelets do not adhere to intact endothelium, but they adhere to the constituents of the subendothelium, release the contents of their granules (including %%%PDGF%%%), and form thromboxanes. If blood flow is disturbed, platelet--fibrin thrombi can form at sites of injury. Platelet adherence to a damaged wall does not require von Willebrand factor except under conditions of high wall shear. Repeated injury of a vessel wall leads to the development of lipid-rich atherosclerotic lesions, even in normocholesterolemic animals, but these lesions do not form if the experimental animals are made thrombocytopenic before injury is induced. Measurable changes in platelets that are associated with the clinical complications of atherosclerosis include shortened survival, release of granule contents (platelet factor 4, beta-thromboglobulin, thrombospondin), formation of thromboxanes, and decreased buoyant density. "Antiplatelet drugs" such as aspirin are proving to be beneficial in selected groups of patients, such as those with unstable angina. Thromboxane synthetase inhibitors and agents that block the thromboxane receptor on platelets are under investigation. Long term administration of "antiplatelet drugs" to affect the rate of development of atherosclerosis seems neither feasible nor desirable. Modification of dietary and smoking habits and control of hypertension are more likely to be beneficial for most individuals.

? ds

Set	Items	Description
S1	115	PDGF AND (ANTIBODIES OR ANTIBODY) AND CELL()PROLIF?
S2	73	S1 AND PY>1991
S3	42	S1 NOT S2
S4	28	S3 NOT PY=1991

? s s3 and py=1991

	42	S3
	375769	PY=1991
S5	14	S3 AND PY=1991

? t s5/6/all

5/6/1
07447596 91317881

Prolactin induces proliferation of vascular smooth muscle cells through a protein kinase C-dependent mechanism.

5/6/2
07062558 92157456
Demonstration of %%%PDGF%%% B-chain mRNA in glomeruli in mesangial proliferative nephritis by in situ hybridization.

5/6/3
07054419 91350644
Platelet-derived growth factor expression in mesangial proliferative glomerulonephritis.

5/6/4
06999114 92035724
Mitogenic effect of platelet-derived growth factor in human glomerular mesangial cells: modulation and/or suppression by inflammatory cytokines.

5/6/5
06991456 91303230
Response of low-passage human malignant gliomas in vitro to stimulation and selective inhibition of growth factor-mediated pathways.

5/6/6
06961833 91123433
Platelet-derived growth factor activity and mRNA expression in healing vascular grafts in baboons. Association in vivo of platelet-derived growth factor mRNA and protein with cellular proliferation.

5/6/7
06946539 92231287
Adhesion molecules in skin development: morphogenesis of feather and hair.

5/6/8
06876876 92068527
Differential proliferation of rat lung fibroblasts induced by the platelet-derived growth factor-AA, -AB, and -BB isoforms secreted by rat alveolar macrophages [see comments]

5/6/9
06826519 91300732
Differential control of mesangial %%%cell%%% %%%proliferation%%% by interferon-gamma.

5/6/10
06815172 91373393
Effects of platelet-derived growth factor and transforming growth factor-beta 1 on the synthesis of a large versican-like chondroitin sulfate proteoglycan by arterial smooth muscle cells.

5/6/11
06744778 91253610

Regulation of mesangial %%%cell%%% %%%proliferation%%%.

5/6/12
06725374 91217107
Uric acid stimulates vascular smooth muscle %%%cell%%% %%%proliferation%%% by increasing platelet-derived growth factor A-chain expression.

5/6/13
06696579 91127978
[Microbiological approach to the treatment of brain tumors]

5/6/14
06692038 91105999
Production by cultured human monocytes of mesangial %%%cell%%% %%%proliferation%%% factor(s) differing from interleukin-1 and interleukin-6.
? t s5/6/allds

>>>'ALLDS' not recognized as item list
? ds

Set Items Description
S1 115 PDGF AND (ANTIBODIES OR ANTIBODY) AND CELL()PROLIF?
S2 73 S1 AND PY>1991
S3 42 S1 NOT S2
S4 28 S3 NOT PY=1991
S5 14 S3 AND PY=1991
? s pdgf and (antibodies or antibody) not s1

4151 PDGF
316183 ANTIBODIES
315260 ANTIBODY
115 S1
S6 683 PDGF AND (ANTIBODIES OR ANTIBODY) NOT S1
? s s6 and py>1991

683 S6
2132219 PY>1991
S7 431 S6 AND PY>1991
? s s6 not s7

683 S6
431 S7
S8 252 S6 NOT S7
? t s8/kwic/

8/KWIC/1
DIALOG(R)File 155:(c) format only 1997 Knight-Ridder Info. All rts. reserv.

Use of monoclonal %%%antibodies%%% as probes for oncogene products.
Descriptors: %%%Antibodies%%%, Monoclonal--Diagnostic Use--DU; *Neoplasm Proteins--Analysis--AN; *Oncogenes; *Proto-Oncogene Proteins--Analysis--AN
...Gene Symbol: sea; MET; PKC I/PKC II; PKC III; capk; CDC 28; TRK; RET; EPH; RAF-1; PKS; pim-1; MOS; cgpk; HER-1/HER-2; %%%PDGF%%%-R; FMS/KIT; ROS/sev; HIR/HILR; ABL; mlck; LYN/lck/tk1; HCK
Chemical Name: %%%Antibodies%%%, Monoclonal; (Neoplasm Proteins; (Proto-Oncogene Proteins

? t s8/kwic/2-10

8/KWIC/2
DIALOG(R)File 155:(c) format only 1997 Knight-Ridder Info. All rts. reserv.

Platelet-derived growth factor-mediated Ca2+ entry is blocked by %%%antibodies%%% to phosphatidylinositol 4,5-bisphosphate but does not involve heparin-sensitive inositol 1,4,5-trisphosphate receptors.
Elevation of intracellular Ca2+ by platelet-derived growth factor (%%%PDGF%%%) and other growth factors involves both release of Ca2+ from intracellular Ca2+ stores and Ca2+ entry from the extracellular medium. Release from intracellular stores is...

... inositol 1,4,5-trisphosphate (IP3) and the heparin-sensitive IP3 receptor. We studied the mechanism by which entry of extracellular Ca2+ is induced by %%%PDGF%%% . Intracellular free Ca2+ (Ca2+i) was measured in single cultured rat vascular smooth muscle cells using fura 2 microspectrofluorometry. In nominally Ca2(+)-free medium, %%%PDGF%%% (recombinant BB, 10 ng/ml) raised intracellular Ca2+ transiently (less than 5 min); addition of 2 mM Ca2+ to the bathing medium after 5 min...

... in response to changes in extracellular Ca2+ was virtually undetectable in control or thrombin-treated cells. The intracellular response to changes in medium Ca2+ after %%%PDGF%%% was completely blocked by 10 mM CoCl2, but not by 10(-7) M nicardipine. Microinjection of monoclonal %%%antibodies%%% to phosphatidylinositol 4,5-bisphosphate (PIP2) (kt 10, 2 mg/ml) totally abolished both mobilization of intracellular Ca2+ stores and entry of extracellular Ca2+. Consistent with this finding, maintenance of Ca2+ entry required ongoing receptor occupancy, since displacement of %%%PDGF%%% from its receptor with suramin (1 mM) eradicated extracellular Ca2+ entry in less than 5 min. To determine whether extracellular Ca2+ entry involves the heparin-sensitive IP3 receptor, cells were microinjected with heparin (4 mg/ml) prior to addition of %%%PDGF%%% . Heparin, but not chondroitin sulfate, prevented mobilization of intracellular Ca2+ stores but did not affect extracellular Ca2+ entry. We %%%PDGF%%% requires ongoing receptor occupancy and involves PIP2 or PIP2 metabolism. However, the signal which mediates %%%PDGF%%% -induced Ca2+ entry does not require the heparin-sensitive IP3 receptor.

8/KWIC/3
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...times the proto-oncogene level) and are accompanied by large increases in the steady state mRNA levels of transin and TGF-alpha and decreases in %%%PDGF%%% -receptor mRNA and fibronectin protein and mRNA levels. In addition, the level of a novel cytoplasmic protein species (referred to as p29), which is stained by a monoclonal %%%antibody%%% for ras, is dramatically reduced in response to these levels of activated ras protein. Thus changes in morphology and gene expression induced by rasT24 occur...

8/KWIC/4
DIALOG(R)File 155:(c) format only 1997 Knight-Ridder Info. All rts. reserv.

Antiproliferative effect of trapidil on %%%PDGF%%%-associated growth of human glioma cell lines in vitro.
The effects of trapidil on platelet-derived growth factor (%%%PDGF%%%)-associated growth of glioblastoma cells were studied. The assessment using %%%PDGF%%%-dependent rat lung endothelium cells revealed secretion of a %%%PDGF%%% -like factor from SF-126 cell line but not from SF-188. Human recombinant %%%PDGF%%% stimulated proliferation of both these glioblastoma

cell lines. The anti-%%%PDGF%%% monoclonal %%%antibody%%% inhibited the growth of SF-126 more than SF-188. The results suggest the presence of an autocrine growth mechanism in SF-126 cells mediated by %%%PDGF%%%. The growth of both SF-126 and SF-188 cells was suppressed by trapidil, a specific %%%PDGF%%% antagonist, at 10 and 50 micrograms/ml, respectively. The proliferative response to exogenous %%%PDGF%%% and the antagonistic effect of trapidil were greater in the SF-126 cell line. In addition, trapidil markedly reduced production of prostaglandin E2 in both...
; %%%Antibodies%%%, Monoclonal--Immunology--IM; Biological Assay; Cell Division--Drug Effects--DE; Cells, Cultured; Dinoprostone--Biosynthesis--BI ; Epithelium--Cytology--CY; Neoplasm Proteins--Biosynthesis--BI; Neoplasm Proteins--Secretion...
Chemical Name: %%%Antibodies%%%, Monoclonal; (Neoplasm Proteins; (Platelet-Derived Growth Factor; (Recombinant Proteins; (Transforming Growth Factor beta; (Trapidil; (Dinoprostone

8/KWIC/5

In the present study, the relations between acidic and basic fibroblast growth factors (aFGF and bFGF, respectively), platelet-derived growth factor (%%%PDGF%%%), and food intake were studied. When aFGF-, bFGF-, and %%%PDGF%%% -like activity in cerebrospinal fluid (CSF) was examined by bioassay, the activity of those factors significantly increased in postfeeding CSF, compared to prefeeding CSF. Injections of aFGF, bFGF, aFGF (synthetic amino-terminal peptide of aFGF), and %%%PDGF%%% into the third cerebral ventricle decreased food intake, and injections of anti-aFGF, anti-bFGF, and anti-aFGF %%%antibodies%%% into the lateral hypothalamus (LHA) increased food intake. The activity of LHA glucose-sensitive neurons was inhibited by electrophoretic application of aFGF. These results suggest that aFGF, bFGF and %%%PDGF%%% have in vivo physiological roles in the central nervous system, distinct from those as mitogens.
; %%%Antibodies%%%--Administration and Dosage--AD; %%%Antibodies%%% --Physiology--PH; Brain--Physiology--PH; Chemoreceptors--Drug Effects--DE; Fibroblast Growth Factor, Acidic--Cerebrospinal Fluid--CF; Fibroblast Growth Factor, Acidic--Immunology--IM; Fibroblast Growth Factor...
Chemical Name: %%%Antibodies%%%; (Fibroblast Growth Factor, Basic; (Peptide Fragments; (Platelet-Derived Growth Factor; (Fibroblast Growth Factor, Acidic

8/KWIC/6

Phosphotyrosine %%%antibodies%%% as probes for activated oncogene products endowed with tyrosine kinase activity.
The usefulness of phosphotyrosine %%%antibodies%%% for the detection of physiologically regulated or deregulated kinases is shown in this paper. This rather rare enzymatic activity is shared by receptors for some polypeptide growth factors and by the products of class 1 oncogenes. The %%%antibodies%%% are able to detect proteins phosphorylated on tyrosine in fibroblasts stimulated with growth factors, such as EGF and %%%PDGF%%%. The major phosphorylated protein species are the receptors themselves, which undergo phosphorylation only following the addition of the exogenous factor and only transiently. Phosphotyrosine %%%antibodies%%% were able to detect the products of the retroviral class 1 oncogenes, which are endowed of deregulated tyrosine kinase activity. In fact, in these cases...

... independently of the presence or lack of the growth factor. A tyrosine kinase constitutively activated in human gastric carcinoma cells was detected by P-Tyr %%%antibodies%%%. This molecule has been characterized at molecular level and the mechanisms responsible for its enzymatic activation

has been investigated. The question of whether the tyrosine...

... of EGF receptors or deregulated activity of c-abl encoded proteins in CML and ALL. Thus, the search for deregulated kinases by means of phosphotyrosine %%%antibodies%%% seems to be useful for identifying new activated oncogenes in clinical oncology.
Descriptors: %%%Antibodies%%%--Immunology--IM; *Growth Substances --Analysis--AN; *Oncogene Proteins--Analysis--AN; *Protein-Tyrosine Kinase --Analysis--AN; *Proto-Oncogene Proteins--Analysis--AN; *Receptors, Cell Surface--Analysis--AN...
Chemical Name: Protein-Tyrosine Kinase; (%%%Antibodies%%%; (Growth Substances; (Membrane Proteins; (Oncogene Proteins; (Proto-Oncogene Proteins; (Receptors, Cell Surface; (Tumor Markers, Biological; (Phosphotyrosine; (Tyrosine

8/KWIC/7
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...specific increase in neurite outgrowth of dorsal root ganglion neurons on the astrocyte substrate. L1 expression induced by TGF-beta was inhibited by addition of %%%antibodies%%% to NGF, suggesting that TGF-beta influences L1 expression by modulating production of NGF by astrocytes. TGF-beta 1 and -beta 2 decreased expression of N-CAM by immature astrocytes. Since N-CAM expression was not affected by NGF and %%%antibodies%%% to NGF did not abolish the TGF-beta-induced decrease in N-CAM expression, NGF did not appear to be the mediator for regulating expression...

... found in the culture supernatants. Addition of interferon-gamma (IFN-gamma), interleukin-1 beta (IL-1 beta), interleukin-6 (IL-6), platelet-derived growth factor (%%%PDGF%%%), or basic fibroblast growth factor (bFGF) to the cultures did not change recognition molecule expression. REcognition molecule expression by mature astrocytes was not found to...

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...demonstrate that the LDL receptor pathway regulates cellular levels of free arachidonic acid (AA) and hence prostaglandin (PG) synthesis. We used platelet-derived growth factor (%%%PDGF%%%)-stimulated fibroblasts as a model system to investigate mechanism of LDL-dependent PG synthesis. %%%PDGF%%% -stimulated but not quiescent cells formed radiolabelled prostacyclin (PGI2) and PGE2 upon incubation with LDL that had been reconstituted with cholesteryl-(1-14C)-arachidonate (rec...

... phenotype of familial hypercholesterolaemia (FH) failed to synthesize significant amounts of PGs. Furthermore cells that had been preincubated with chloroquine or an anti LDL receptor %%%antibody%%%, that prevents binding of LDL to its receptor, did not produce significant amounts of PGs upon incubation with rec-LDL. Moreover incubation of %%%PDGF%%%-stimulated cells with LDL or AA led to a time and concentration-dependent inactivation of PGH synthase, the rate limiting enzyme of PG synthesis. When...

8/KWIC/9
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A crossreactive antipeptide monoclonal %%%antibody%%% with specificity for lysyl-lysine [published erratum appears in J Immunol Methods 1992 May 18;149(2):267]
Synthetic peptides meeting certain guidelines have been used as

immunogens to generate %%%antibodies%%% with predefined specificity. We have raised and characterized using established methods a monoclonal %%%antibody%%% against a synthetic peptide corresponding to the 18-amino acid carboxyterminal sequence (A194-211) of the platelet-derived growth factor (%%%PDGF%%%) A chain expressed by the U343 human glioma cell line. This %%%antibody%%% was generated in order to carry out structure-function studies on this region of %%%PDGF%%% whose biological significance is not yet clear. Anti-%%%PDGF%%%-A194-211 was found to be a low titre, IgM kappa molecule, with a Kd of 2.8 x 10(-7) M. When %%%antibody%%% reactivity was tested with parent %%%PDGF%%% -AAL (A chain homodimer containing a carboxyterminal extension) significant binding was observed. Surprisingly, 125I-%%%PDGF%%% -AAS, consisting of truncated A chains but lacking the extension was also bound. Moreover, poly-L-lysine, beta-thromboglobulin, %%%PDGF%%%-A194-211, and myoglobin competed dose-dependently with 125I-%%%PDGF%%%-AAL for %%%antibody%%% . 125I-bovine serum albumin was also bound. Examination of the primary sequence of proteins and peptides bound by the %%%antibody%%% revealed only one shared structural motif: a lysyl-lysine moiety. Selected small synthetic peptides containing this and other sequences were used as potential competitors of 125I-%%%PDGF%%% -A194-211 in %%%antibody%%% binding. Lysyl-lysyl-glycyl-glutamic acid [corrected] and lysyl-lysine competed, whereas lysyl-leucine did not. These results suggest that as few as two amino...

... the minimum number of residues required. Furthermore, we show that guidelines governing the design of synthetic peptides for their use as antigens to produce monoclonal %%%antibodies%%% of predetermined specificity may be unreliable.

Descriptors: %%%Antibodies%%%, Monoclonal--Immunology--IM; *Dipeptides --Immunology--IM; Amino Acid Sequence; %%%Antibody%%% Specificity; Binding, Competitive; Cross Reactions; Epitopes; Immunoglobulin Isotypes--Immunology --IM; Mice; Mice, Inbred BALB C; Molecular Sequence Data; Peptides --Chemistry--CH; Peptides--Immunology--IM; Platelet...

Chemical Name: %%%Antibodies%%%, Monoclonal; (Dipeptides; (Epitopes; (Immunoglobulin Isotypes; (Peptides; (Platelet-Derived Growth Factor; (lysyllysine

8/KWIC/10

The human breast cancer cell lines T47D and MCF-7, respond to the mitogenic action of exogenously added %%%PDGF%%% with a 2-3-fold increase in cell number. The maximal response was obtained at a concentration of 1.25 half maximal units/ml (125 ng/ml). %%%PDGF%%% -AA was even more effective than %%%PDGF%%%-AB while %%%PDGF%%%-BB was without effect. The growth-enhancing activity of %%%PDGF%%% was completely abolished by Fab fragments of anti %%%PDGF%%%. Within 7 min of addition of %%%PDGF%%% to cultures of T47D cells, specific phosphorylation of a 65-kDa protein was observed. T47D cells contain specific receptors for %%%PDGF%%% with approximately 4-7 x 10(4) sites (kDa of 3-4 x 10(-10) M) per cell.

; %%%Antibodies%%%--Pharmacology--PD; Breast Neoplasms--Metabolism--ME; Calcium-Binding Proteins--Antagonists and Inhibitors--AI; Cell Division --Drug Effects--DE; Immunoglobulins, Fab--Pharmacology--PD; Phosphorylation ; Platelet-Derived...

Chemical Name: Annexins; (%%%Antibodies%%%; (Calcium-Binding Proteins; (Immunoglobulins, Fab; (Platelet-Derived Growth Factor; (Receptors, Cell Surface; (Receptors, Platelet-Derived Growth Factor; (Phosphotyrosine; (Tyrosine

? t s8/kwic/11-20

8/KWIC/11

Interleukin 6 stimul[redacted]es growth of vascular s[redacted]oth muscle cells in a %%%PDGF%%%-dependent manner.
... VSMC was totally inhibited by the Ca2+ channel blocker verapamil; however, IL-6 showed no effects on the intracellular Ca2+ level ([Ca2+]i) in VSMC. %%%Antibody%%% against platelet-derived growth factor (%%%PDGF%%%) also totally inhibited the IL-6-induced thymidine uptake. %%%PDGF%%% caused a significant increase in the [Ca2+]i, which was totally inhibited by verapamil. IL-6 mRNA was not detected in unstimulated "quiescent" VSMC, but its expression was stimulated by exposure of VSMC to 10% fetal bovine serum. Immunohistochemical study using anti-%%%PDGF%%% %%%antibody%%% showed that IL-6 stimulated %%%PDGF%%% production in VSMC. These results support the premise that IL-6 is released by VSMC in an autocrine manner and promotes the growth of VSMC via induction of endogenous %%%PDGF%%% production.
; %%%Antibodies%%%--Immunology--IM; Calcium--Metabolism--ME; Cell Division--Drug Effects--DE; Immunohistochemistry--Methods--MT; Interleukin-6--Genetics--GE; Muscle, Smooth, Vascular--Metabolism--ME; Osmolar Concentration; Platelet...
Chemical Name: %%%Antibodies%%%; (Interleukin-6; (Platelet-Derived Growth Factor; (RNA, Messenger; (Calcium

8/KWIC/12
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Platelet-derived growth factor (%%%PDGF%%%) stimulates %%%PDGF%%% receptor subunit dimerization and intersubunit trans-phosphorylation.
High affinity binding of platelet-derived growth factor (%%%PDGF%%%) has been proposed to involve the interaction of the dimeric %%%PDGF%%% ligand with two receptor subunits, designated alpha and beta. We have cloned and expressed a human %%%PDGF%%% receptor cDNA which differs in sequence from the beta-subunit and which has the %%%PDGF%%% binding properties and monoclonal %%%antibody%%% recognition, predicted for the alpha-subunit. Scatchard analysis indicated that %%%PDGF%%%-AA and %%%PDGF%%%-AB bound to transfected alpha-subunits with affinities of Kd = 0.06 and 0.05 nM, respectively. %%%PDGF%%%-BB bound with a significantly lower affinity (Kd = 0.4 nM). Nevertheless, this affinity is still great enough to mediate substantial %%%PDGF%%%-BB binding at physiological concentrations and would be considered to be "high affinity." We have used wild-type and kinase-inactive human beta-subunits to show that %%%PDGF%%% binding promotes receptor subunit dimerization in intact cells. In addition, we found that %%%PDGF%%% stimulates tyrosine phosphorylation of the kinase-inactive beta-subunit when it is expressed with alpha-subunits. The kinase-inactive beta-subunits were phosphorylated at tyrosine...

8/KWIC/13
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Production of platelet derived growth factor B chain (%%%PDGF%%%-B/c-sis) mRNA and immunoreactive %%%PDGF%%% B-like polypeptide by rheumatoid synovium: coexpression with heparin binding acidic fibroblast growth factor-1.
We present evidence supporting the hypothesis that locally produced platelet derived growth factor (%%%PDGF%%%) B-like polypeptides, as well as heparin binding growth factor-1 (HBGF-1), are involved in stimulating the pronounced hyperplasia of rheumatoid synovial stromal fibroblastlike cells. Explanted rheumatoid synovial tissues in vitro spontaneously secreted, in a time dependent manner, mitogenic activity for rheumatoid synoviocytes that was neutralizable by anti-%%%PDGF%%% %%%antibody%%%. %%%PDGF%%% B/c-sis mRNA transcripts were detected in synovium from patients with rheumatoid arthritis (RA) (n = 5). Spontaneous %%%PDGF%%% B-like synthesis was

detected by immunoprecipitation of radiolabeled %%%PDGF%%% B-like polypeptides secreted by explanted tissues. Furthermore, rheumatoid synovial tissues, particularly macrophage-like cells, immunostained specifically with anti-%%%PDGF%%% B chain. The extent and intensity of staining and mononuclear cell infiltration were highly correlated. Immunostaining of osteoarthritic and normal synovial tissues was significantly less than RA synovium. %%%PDGF%%% -B immunostaining of synovial specimens previously characterized for expression of HBGF-1, the precursor of acidic fibroblast growth factor (aFGF), revealed that the extent and intensity of expression of HBGF-1 and %%%PDGF%%%-B were highly correlated.

8/KWIC/14

Cyclic AMP agonists induce the phosphorylation of phospholipase C-tau and of a 76 kDa protein co-precipitated by anti-(phospholipase C-tau) monoclonal %%%antibodies%%% in BALB/c-3T3 cells. Relationship to inositol phosphate formation.

... have demonstrated enhanced phosphorylation of phospholipase C-tau (PLC-tau), a key regulatory enzyme in phosphoinositide metabolism, in cells treated with platelet-derived growth factor (%%%PDGF%%%) and epidermal growth factor, both of which act via specific receptor tyrosine kinases. Our studies on BALB/c-3T3 cells show that agents that promote...

... of cells with cyclic AMP agonists also enhanced, with similar kinetics, the phosphorylation of a 76 kDa protein co-precipitated by anti-PLC-tau monoclonal %%%antibodies%%%. Brief exposure of cells to cholera toxin/IBMX or forskolin/IBMX decreased inositol phosphate formation induced by the GTP-binding protein (G-protein) activator aluminium fluoride by approx. 50%, but was without effect on %%%PDGF%%%-stimulated inositol phosphate formation. These findings suggest that PLC-tau, and perhaps the 76 kDa co-precipitated protein, are substrates of cyclic AMP-dependent protein kinase in BALB/c-3T3 cells: however, the lack of effect of cyclic AMP elevation on %%%PDGF%%%-stimulated inositol phosphate formation indicates that the intrinsic activity of PLC-tau is unaltered by cyclic AMP-mediated phosphorylation.

; Amino Acids--Analysis--AN; %%%Antibodies%%%, Monoclonal--Diagnostic Use --DU; Cell Line; Cholera Toxin--Pharmacology--PD; Kinetics; Mice; Mice, Inbred BALB C; Molecular Weight; Phosphorylation; Platelet-Derived Growth Factor--Pharmacology--PD

Chemical Name: Phospholipase C; (Amino Acids; (%%%Antibodies%%% , Monoclonal; (Inositol Phosphates; (Phosphoproteins; (Platelet-Derived Growth Factor; (1-Methyl-3-isobutylxanthine; (Cyclic AMP; (Forskolin; (Cholera Toxin

8/KWIC/15

... important mediators of the inflammatory lesions and consequent interstitial fibrosis caused by inhalation of inorganic particles. Identification of a homolog of platelet-derived growth factor (%%%PDGF%%%) produced by rat alveolar macrophages that were stimulated with carbonyl iron particles and asbestos fibers motivated our studies on the biologic activity of this potent cytokine. Macrophage-derived %%%PDGF%%% (MD-%%%PDGF%%%) competes for specific membrane receptors on rat lung fibroblasts, initiating DNA synthesis and cell replication. The present report demonstrates that purified human %%%PDGF%%% and the MD-%%%PDGF%%% are chemotactic for early passage rat lung fibroblasts, but not for lung macrophages. Rat lung fibroblasts exhibit a typical bell-shaped, dose-related curve and respond optimally between 2 and 4 ng/ml %%%PDGF%%%.

We found that alveolar macrophage-conditioned medium (AMCM), fractionated by gel filtration in 1 [redacted]acetic acid, induced a cl[redacted] chemotactic response in the same fractions (20 to 22 ml) where %%%PDGF%%% was identified by enzyme immunoassay. In contrast, AMCM fractionated by gel filtration in phosphate-buffered saline did not induce any chemotactic activity unless the fractions...

... with molecular weights of 150 and greater than 200 kD. All chemotactic activity observed with fractionated AMCM was blocked greater than 90% by an anti-%%%PDGF%%% %%%antibody%%%. These observations demonstrate that MD-%%%PDGF%%% is chemotactic for rat lung fibroblasts if it first is released from its binding protein, alpha-macroglobulin (alpha-M), which is secreted into the medium along with %%%PDGF%%%.(ABSTRACT TRUNCATED AT 250 WORDS)

8/KWIC/16

... 1. IL-1-stimulated synovial cells were shown to secrete biologically active GM-CSF and G-CSF, which were specifically inhibited by their respective monoclonal %%%antibodies%%% . The transcription inhibitor, actinomycin D, and protein synthesis inhibitor, cycloheximide, inhibited the increase in GM-CSF and G-CSF production induced by IL-1 and TNF. Finally, other cytokines, IL-3, interferon gamma (IFN gamma), IL-2, platelet-derived growth factor (%%%PDGF%%%), epidermal growth factor (EGF) and transforming growth factor alpha (TGF alpha), failed to stimulate either GM-CSF or G-CSF production, whether alone or in...

8/KWIC/17

A small v-sis/platelet-derived growth factor (%%%PDGF%%%) B-protein domain in which subtle conformational changes abrogate %%%PDGF%%% receptor interaction and transforming activity.

...by antisera which detect determinants dependent upon native intrachain disulfide linkages, yet the same mutations completely abolished transforming activity. A platelet-derived growth factor B (%%%PDGF%%% B) monoclonal %%%antibody%%% that prevents its interaction with %%%PDGF%%% receptors recognized v-sis, delta 142 (deletion of codon 142), and delta 148 but not delta 136, delta 137, or delta 139 mutants. These findings mapped the epitope recognized by this monoclonal %%%antibody%%% to include amino acid residues 136 to 139. Furthermore, mutations in the codon 136 to 148 domain caused markedly impaired ability to induce %%%PDGF%%% receptor tyrosine phosphorylation. Thus, subtle conformational alterations in this small domain critically affect %%%PDGF%%% receptor recognition and/or functional activation.

; %%%Antibodies%%%, Monoclonal--Immunology--IM; Cell Transformation, Neoplastic; Codon; DNA Mutational Analysis; Epitopes; Mice; Tyrosine --Analogs and Derivatives--AA; Tyrosine--Metabolism--ME

Chemical Name: oncogene proteins sis; (%%%Antibodies%%%, Monoclonal; (Codon; (Epitopes; (Platelet-Derived Growth Factor; (Receptors, Cell Surface; (Receptors, Platelet-Derived Growth Factor; (Retroviridae Proteins, Oncogenic; (Phosphotyrosine; (Tyrosine

8/KWIC/18

Association between the %%%PDGF%%% receptor and members of the src family of tyrosine kinases.

We have examined the interaction between the platelet-derived growth factor (%%%PDGF%%%) receptor and three src family tyrosine kinases,

pp60c-src, p59fyn, and pp62c-yes. The kinase activities of all three enzymes were elevated after %%%PDGF%%% stimulation of quiescent fibroblasts, coincident with association of the src family kinases with the %%%PDGF%%% receptor and other proteins. The presence of a protein of 81-85 kd in these complexes correlated with the detection of phosphatidylinositol (PI) kinase activity (previously described to associate with both the %%%PDGF%%% receptor and pp60c-src-middle T antigen). These results suggest that the physiological response to %%%PDGF%%% involves interaction of the receptor not only with serine/threonine and lipid kinases and a phospholipase, but also with other tyrosine kinases.
; Amino Acid Sequence; %%%Antibodies%%%; Blotting, Western; Cell Line; Enzyme Activation; Mice; Molecular Sequence Data; Platelet-Derived Growth Factor--Metabolism--ME; Protein Binding
Chemical Name: Proto-Oncogene Protein pp60(c-src); (Protein-Tyrosine Kinase; (proto-oncogene protein c-fyn; (proto-oncogene protein c-yes; (%%%Antibodies%%%; (Platelet-Derived Growth Factor; (Proto-Oncogene Proteins ; (Receptors, Cell Surface; (Receptors, Platelet-Derived Growth Factor

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... reaches a maximum after 2 hr at 4 degrees C. The 175 kDa protein phosphorylated in vivo at low temperatures can be immunoprecipitated by phosphotyrosine %%%antibodies%%% and displays auto-kinase activity in vitro in the presence of radiolabelled ATP. This molecule was found to react with anti-peptide %%%antibodies%%% directed against the product of the HER2/neu proto-oncogene only when immunoprecipitated with phosphotyrosine %%%antibodies%%% from cold-stimulated cells. Activation of protein kinase-C by treatment of the cells with phorbol esters, bombesin or %%%PDGF%%% inhibits the effect of the exposure to low temperatures. Phosphorylation of p175 is not induced by treatment of the cells with the phosphatases inhibitor sodium...

8/KWIC/20
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... a putative p185neu-specific ligand is produced by macrophages activated by MDP. Using MDP-CM, the presence of a 25 kDa polypeptide distinct from EGF, %%%PDGF%%% , FGF, IGF, TGF-alpha and TGF-beta and TNF-alpha, could be demonstrated by decorating a Western blot with soluble NEU and anti-NEU %%%antibodies%%% . Thus, a 25 kDa (non-reduced) p185neu ligand has been described.

```
? s s8 and anti()pdgf

            252  S8
         244832  ANTI
           4151  PDGF
            169  ANTI(W)PDGF
      S9     40  S8 AND ANTI()PDGF
? t s9/kwic/1-10
```

9/KWIC/1
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Antiproliferative effect of trapidil on %%%PDGF%%%-associated growth of human glioma cell lines in vitro.
The effects of trapidil on platelet-derived growth factor (%%%PDGF%%%)-associated growth of glioblastoma cells were studied. The assessment using %%%PDGF%%%-dependent rat lung endothelium cells revealed secretion of a %%%PDGF%%% -like factor from SF-126 cell line but not from SF-188. Human

recombinant %%%PDGF%%% stimulated proliferation of both these glioblastoma cell lines. The %%%anti-%%%PDGF%%% monoclonal %%%antibody%%% inhibited the growth of SF-126 more than SF-188. The results suggest the presence of an autocrine growth mechanism in SF-126 cells mediated by %%%PDGF%%%. The growth of both SF-126 and SF-188 cells was suppressed by trapidil, a specific %%%PDGF%%% antagonist, at 10 and 50 micrograms/ml, respectively. The proliferative response to exogenous %%%PDGF%%% and the antagonistic effect of trapidil were greater in the SF-126 cell line. In addition, trapidil markedly reduced production of prostaglandin E2 in both...
; %%%Antibodies%%%, Monoclonal--Immunology--IM; Biological Assay; Cell Division--Drug Effects--DE; Cells, Cultured; Dinoprostone--Biosynthesis--BI ; Epithelium--Cytology--CY; Neoplasm Proteins--Biosynthesis--BI; Neoplasm Proteins--Secretion...
Chemical Name: %%%Antibodies%%%, Monoclonal; (Neoplasm Proteins; (Platelet-Derived Growth Factor; (Recombinant Proteins; (Transforming Growth Factor beta; (Trapidil; (Dinoprostone

9/KWIC/2

A crossreactive antipeptide monoclonal %%%antibody%%% with specificity for lysyl-lysine [published erratum appears in J Immunol Methods 1992 May 18;149(2):267]
Synthetic peptides meeting certain guidelines have been used as immunogens to generate %%%antibodies%%% with predefined specificity. We have raised and characterized using established methods a monoclonal %%%antibody%%% against a synthetic peptide corresponding to the 18-amino acid carboxyterminal sequence (A194-211) of the platelet-derived growth factor (%%%PDGF%%%) A chain expressed by the U343 human glioma cell line. This %%%antibody%%% was generated in order to carry out structure-function studies on this region of %%%PDGF%%% whose biological significance is not yet clear. %%%Anti%%%-%%%PDGF%%%-A194-211 was found to be a low titre, IgM kappa molecule, with a Kd of 2.8 x 10(-7) M. When %%%antibody%%% reactivity was tested with parent %%%PDGF%%% -AAL (A chain homodimer containing a carboxyterminal extension) significant binding was observed. Surprisingly, 125I-%%%PDGF%%% -AAS, consisting of truncated A chains but lacking the extension was also bound. Moreover, poly-L-lysine, beta-thromboglobulin, %%%PDGF%%%-A194-211, and myoglobin competed dose-dependently with 125I-%%%PDGF%%%-AAL for %%%antibody%%% . 125I-bovine serum albumin was also bound. Examination of the primary sequence of proteins and peptides bound by the %%%antibody%%% revealed only one shared structural motif: a lysyl-lysine moiety. Selected small synthetic peptides containing this and other sequences were used as potential competitors of 125I-%%%PDGF%%% -A194-211 in %%%antibody%%% binding. Lysyl-lysyl-glycyl-glutamic acid [corrected] and lysyl-lysine competed, whereas lysyl-leucine did not. These results suggest that as few as two amino...

... the minimum number of residues required. Furthermore, we show that guidelines governing the design of synthetic peptides for their use as antigens to produce monoclonal %%%antibodies%%% of predetermined specificity may be unreliable.
Descriptors: %%%Antibodies%%%, Monoclonal--Immunology--IM; *Dipeptides --Immunology--IM; Amino Acid Sequence; %%%Antibody%%% Specificity; Binding, Competitive; Cross Reactions; Epitopes; Immunoglobulin Isotypes--Immunology --IM; Mice; Mice, Inbred BALB C; Molecular Sequence Data; Peptides --Chemistry--CH; Peptides--Immunology--IM; Platelet...
Chemical Name: %%%Antibodies%%%, Monoclonal; (Dipeptides; (Epitopes; (Immunoglobulin Isotypes; (Peptides; (Platelet-Derived Growth Factor; (lysyllysine

9/KWIC/3

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The human breast cancer cell lines T47D and MCF-7, respond to the mitogenic action of exogenously added %%%PDGF%%% with a 2-3-fold increase in cell number. The maximal response was obtained at a concentration of 1.25 half maximal units/ml (125 ng/ml). %%%PDGF%%% -AA was even more effective than %%%PDGF%%%-AB while %%%PDGF%%%-BB was without effect. The growth-enhancing activity of %%%PDGF%%% was completely abolished by Fab fragments of %%%anti%%% %%%PDGF%%%. Within 7 min of addition of %%%PDGF%%% to cultures of T47D cells, specific phosphorylation of a 65-kDa protein was observed. T47D cells contain specific receptors for %%%PDGF%%% with approximately 4-7 x 10(4) sites (kDa of 3-4 x 10(-10) M) per cell.

; %%%Antibodies%%%--Pharmacology--PD; Breast Neoplasms--Metabolism--ME; Calcium-Binding Proteins--Antagonists and Inhibitors--AI; Cell Division --Drug Effects--DE; Immunoglobulins, Fab--Pharmacology--PD; Phosphorylation ; Platelet-Derived...

Chemical Name: Annexins; (%%%Antibodies%%%; (Calcium-Binding Proteins; (Immunoglobulins, Fab; (Platelet-Derived Growth Factor; (Receptors, Cell Surface; (Receptors, Platelet-Derived Growth Factor; (Phosphotyrosine; (Tyrosine

9/KWIC/4

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Interleukin 6 stimulates growth of vascular smooth muscle cells in a %%%PDGF%%%-dependent manner.

... VSMC was totally inhibited by the Ca2+ channel blocker verapamil; however, IL-6 showed no effects on the intracellular Ca2+ level ([Ca2+]i) in VSMC. %%%Antibody%%% against platelet-derived growth factor (%%%PDGF%%%) also totally inhibited the IL-6-induced thymidine uptake. %%%PDGF%%% caused a significant increase in the [Ca2+]i, which was totally inhibited by verapamil. IL-6 mRNA was not detected in unstimulated "quiescent" VSMC, but its expression was stimulated by exposure of VSMC to 10% fetal bovine serum. Immunohistochemical study using %%%anti%%%-%%%PDGF%%% %%%antibody%%% showed that IL-6 stimulated %%%PDGF%%% production in VSMC. These results support the premise that IL-6 is released by VSMC in an autocrine manner and promotes the growth of VSMC via induction of endogenous %%%PDGF%%% production.

; %%%Antibodies%%%--Immunology--IM; Calcium--Metabolism--ME; Cell Division--Drug Effects--DE; Immunohistochemistry--Methods--MT; Interleukin-6--Genetics--GE; Muscle, Smooth, Vascular--Metabolism--ME; Osmolar Concentration; Platelet...

Chemical Name: %%%Antibodies%%%; (Interleukin-6; (Platelet-Derived Growth Factor; (RNA, Messenger; (Calcium

9/KWIC/5

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Production of platelet derived growth factor B chain (%%%PDGF%%%-B/c-sis) mRNA and immunoreactive %%%PDGF%%% B-like polypeptide by rheumatoid synovium: coexpression with heparin binding acidic fibroblast growth factor-1.

We present evidence supporting the hypothesis that locally produced platelet derived growth factor (%%%PDGF%%%) B-like polypeptides, as well as heparin binding growth factor-1 (HBGF-1), are involved in stimulating the pronounced hyperplasia of rheumatoid synovial stromal fibroblastlike cells. Explanted rheumatoid synovial tissues in vitro spontaneously secreted, in a time dependent manner, mitogenic activity for rheumatoid synoviocytes that was neutralizable by %%%anti%%%-%%%PDGF%%% %%%antibody%%%. %%%PDGF%%% B/c-sis mRNA transcripts were detected in synovium from patients with rheumatoid arthritis (RA) (n = 5). Spontaneous %%%PDGF%%% B-like synthesis

was detected by immunoprecipitation of radiolabeled %%%PDGF%%% B-like polypeptides secreted by explanted tissues. Furthermore, rheumatoid synovial tissues, particularly macrophage-like cells, immunostained specifically with %%%anti%%%-%%%PDGF%%% B chain. The extent and intensity of staining and mononuclear cell infiltration were highly correlated. Immunostaining of osteoarthritic and normal synovial tissues was significantly less than RA synovium. %%%PDGF%%% -B immunostaining of synovial specimens previously characterized for expression of HBGF-1, the precursor of acidic fibroblast growth factor (aFGF), revealed that the extent and intensity of expression of HBGF-1 and %%%PDGF%%%-B were highly correlated.

9/KWIC/6

... important mediators of the inflammatory lesions and consequent interstitial fibrosis caused by inhalation of inorganic particles. Identification of a homolog of platelet-derived growth factor (%%%PDGF%%%) produced by rat alveolar macrophages that were stimulated with carbonyl iron particles and asbestos fibers motivated our studies on the biologic activity of this potent cytokine. Macrophage-derived %%%PDGF%%% (MD-%%%PDGF%%%) competes for specific membrane receptors on rat lung fibroblasts, initiating DNA synthesis and cell replication. The present report demonstrates that purified human %%%PDGF%%% and the MD-%%%PDGF%%% are chemotactic for early passage rat lung fibroblasts, but not for lung macrophages. Rat lung fibroblasts exhibit a typical bell-shaped, dose-related curve and respond optimally between 2 and 4 ng/ml %%%PDGF%%%. We found that alveolar macrophage-conditioned medium (AMCM), fractionated by gel filtration in 1 M acetic acid, induced a clear chemotactic response in the same fractions (20 to 22 ml) where %%%PDGF%%% was identified by enzyme immunoassay. In contrast, AMCM fractionated by gel filtration in phosphate-buffered saline did not induce any chemotactic activity unless the fractions...

... fractions with molecular weights of 150 and greater than 200 kD. All chemotactic activity observed with fractionated AMCM was blocked greater than 90% by an %%%anti%%%-%%%PDGF%%% %%%antibody%%%. These observations demonstrate that MD-%%%PDGF%%% is chemotactic for rat lung fibroblasts if it first is released from its binding protein, alpha-macroglobulin (alpha-M), which is secreted into the medium along with %%%PDGF%%% .(ABSTRACT TRUNCATED AT 250 WORDS)

9/KWIC/7

Human umbilical vein endothelial (HUVE) cells have been previously reported to express the genes for the A and B chains of %%%PDGF%%% and to secrete %%%PDGF%%%-related factors into culture media. Antihuman %%%PDGF%%% IgG affinity chromatography was used to purify %%%PDGF%%%-related activity from HUVE cell-conditioned media. Immunoblot analysis of the affinity-purified proteins with %%%anti%%%-%%%PDGF%%% IgG and %%%antibodies%%% specific for the A or B chain peptides of %%%PDGF%%% combined with chemotactic and mitogenic assays revealed that the major %%%PDGF%%% immunorelated molecule secreted by HUVE cells is a monomer of approximately 36-38 kD and that less than 10% of the purified biologically active molecules are %%%PDGF%%% A or B chain peptides. Screening of an HUVE cell cDNA library in the expression vector lambda gtl 1 with the %%%anti%%% -%%%PDGF%%% %%%antibody%%% resulted in the cloning and sequencing of a cDNA with an open reading frame encoding a 38-kD cysteine-rich secreted protein which we show to be the major %%%PDGF%%%-related mitogen secreted by human vascular endothelial cells. The protein has a 45% overall homology to the

translation product of the v-src-induced CEF...

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Platelet-derived growth factor (%%%PDGF%%%)-induced disulfide-linked dimerization of %%%PDGF%%% receptor in living cells.
It is well established that epidermal growth factor and platelet-derived growth factor (%%%PDGF%%%) are able to induce noncovalent dimerization of their surface receptors. It is thought that receptor dimerization plays an important role in activation of the tyrosine kinase function and in the process of receptor autophosphorylation. Here we show that the addition of either %%%PDGF%%%-BB or %%%PDGF%%%-AA to intact 3T3 cells induces formation of 400- and 430-kDa species, respectively, recognized by either %%%anti%%%-%%%PDGF%%% receptor %%%antibodies%%% or anti-phosphotyrosine %%%antibodies%%% . Interestingly, the 400- and the 430-kDa species are detected in nonreducing gels but not in reducing gels. Moreover, an alkylating agent, N-ethylmaleimide, inhibits %%%PDGF%%%-induced formation of high-molecular-mass species. Comparisons of V8 protease peptide maps of [35S]methionine-labeled %%%PDGF%%% receptors and high-molecular-mass proteins indicate that they represent dimers of %%%PDGF%%% receptors. It appears therefore that in addition to noncovalent dimerization, %%%PDGF%%% receptors undergo ligand-dependent disulfide-linked dimerization.

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Receptors for platelet-derived growth factor (%%%PDGF%%%) have not been identified previously to our knowledge in human myeloid cells that also produce %%%PDGF%%%. Here we report that phorbol ester-treated myeloid cells differentiated along the monocytic lineage express both a full-length 5.5-kilobase (kb) mRNA and a predominant, truncated 4.6-kb mRNA coding for the %%%PDGF%%% B-chain receptor (%%%PDGF%%%-BR). %%%PDGF%%% -BR was identified in phorbol ester-differentiated myeloid cells by indirect immunofluorescence with an %%%antibody%%% specific to %%%PDGF%%%-BR. This %%%anti%%%-%%%PDGF%%% -BR was also used in immunoprecipitation studies to demonstrate that lysates of phorbol ester-differentiated myeloid cells contain %%%PDGF%%%-BR molecules of 37 kDa to 130 kDa. The results also show that the tandemly linked genes for %%%PDGF%%% -BR and the macrophage colony-stimulating factor 1 receptor are coexpressed in the phorbol ester-differentiated myeloid cells. Expression of these two receptor genes has...
; Cell Line; Fluorescent %%%Antibody%%% Technique; Macromolecular Systems ; Monocytes--Cytology--CY; Monocytes--Physiology--PH; Platelet-Derived Growth Factor--Physiology--PH; Receptors, Cell Surface--Analysis--AN; Receptors, Macrophage Colony-Stimulating Factor...

9/KWIC/10
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... expression of transforming ras (v-ras) can block the stimulation of growth-related gene expression and cell division mediated by the platelet-derived growth factor (%%%PDGF%%%) may provide a model for the functional interation of ras with growth factor receptors. In the current studies, we have demonstrated that this blockade by v-ras of %%%PDGF%%%-BB signal transduction occurs very early in signal transduction, at the level of %%%PDGF%%% receptor autophosphorylation. Although the expression of %%%PDGF%%% receptor as detected by Western blot with %%%anti%%%-%%%PDGF%%% receptor %%%antibody%%% was not diminished in v-ras-transformed murine Balb/c 3T3 fibroblasts, the autophosphorylation of %%%PDGF%%% receptor in

response to ligand (recombinant %%%PDGF%%%-BB homodimer) stimulation was profoundly suppressed. This same phenomenon of v-ras-mediated %%%PDGF%%% receptor autophosphorylation inhibition was also demonstrated in normal rat kidney fibroblasts. Further, factor(s) present in v-ras-expressing fibroblasts found in the membrane fractions of these cells can dominantly inhibit the autophosphorylation of the %%%PDGF%%% receptor obtained from normal fibroblasts. These findings suggest a role for ras in one of the earliest steps of the signal transduction pathway.
? t s9/kwic/11-20

9/KWIC/11

Ligand-induced interaction between alpha- and beta-type platelet-derived growth factor (%%%PDGF%%%) receptors: role of receptor heterodimers in kinase activation.

Two types of %%%PDGF%%% receptors have been cloned and sequenced. Both receptors are transmembrane glycoproteins with a ligand-stimulatable tyrosine kinase site. We have shown earlier that ligand-induced activation of the beta-type %%%PDGF%%% receptor is due to the conversion of the monomeric form of the receptor to the dimeric form [Bishayee et al. (1989) J. Biol. Chem. 264...

... the role of alpha-receptor in the activation of beta-receptor. These studies were conducted with cells that express one or the other type of %%%PDGF%%% receptor as well as with cells that express both types of receptors. Moreover, ligand-binding characteristics of the receptor were confirmed by immunoprecipitation of the receptor-125I-%%%PDGF%%% covalent complex with type-specific %%%anti%%%-%%%PDGF%%% receptor %%%antibodies%%%. These studies revealed that all three isoforms of %%%PDGF%%% bind to alpha-receptor, and such binding leads to dimerization as well as activation of the receptor. In contrast, beta-receptor can be activated only by %%%PDGF%%% BB and not by %%%PDGF%%% AB or %%%PDGF%%% AA. However, by using antipeptide %%%antibodies%%% that are specific for alpha- or beta-type %%%PDGF%%% receptor, we demonstrated that in the presence of alpha-receptor, beta-receptor kinase can be activated by %%%PDGF%%% AB. We present here direct evidence that strongly suggests that such %%%PDGF%%% AB induced activation of beta-receptor is due to the formation of a noncovalently linked alpha-beta receptor heterodimer.

9/KWIC/12

... of alveolar macrophages (AM) obtained by bronchoalveolar lavage has previously shown that AM from normal individuals spontaneously release small amounts of platelet-derived growth factor (%%%PDGF%%%), a chemotactic and growth factor for mesenchymal cells, whereas AM from IPF patients spontaneously release increased amounts of biologically active %%%PDGF%%%, suggesting its involvement in mesenchymal cell accumulation. However, other cells such as endothelial cells and vascular smooth muscle cells can also release %%%PDGF%%% in vitro. In order to specify %%%PDGF%%% location in lung parenchyma, open lung biopsies from normal individuals and IPF patients were examined by immunohistochemistry using an %%%anti%%%-%%%PDGF%%% %%%antibody%%% and by in situ hybridization using %%%PDGF%%% A-chain and B-chain gene probes. In normal as well as in fibrotic lung, %%%PDGF%%% was only present in relation with interstitial macrophages but not with any other inflammatory cells or mesenchymal cells. Furthermore, the percentage of %%%PDGF%%% -positive macrophages in IPF was 3-fold increased in comparison to normal lung. In addition, the percentage of %%%PDGF%%% -positive macrophages was the same in fibrotic and nonfibrotic areas of IPF lungs.(ABSTRACT TRUNCATED AT 250 WORDS)

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... named SMC-derived migration factor (SDMF). This factor stimulated the migration of SMC dose-dependently and its maximum activity was 2-8 times that of %%%PDGF%%% . Checker board analysis showed that SDMF was chemotactic, but not chemokinetic. In further studies, SDMF was found to be inactivated at 100 degrees C for...

... inactivated by mercaptoethanol. This factor was not dialyzable. Molecular weight was approximately 500 kDa by a gel filtration. The activity was not inhibited by an %%%anti%%%-%%%PDGF%%% %%%antibody%%% or a fibronectin antiserum. These data suggest that SDMF is a potent migration factor for SMC and that SDMF is distinct from %%%PDGF%%%, fibronectin or other known migration factors. This autocrine system of secretion of SDMF by SMC and its induction of SMC migration may contribute to intimal...

9/KWIC/14
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... articular cartilage in organ culture. This is the first known physiologic modifier of PPi production by cartilage. We report herein that platelet derived growth factor (%%%PDGF%%%) is not the platelet factor responsible for PPi stimulation and that the active factor is not mitogenic for chondrocytes. %%%PDGF%%% added to the media of articular cartilage explants in the presence of 0.5% (platelet-poor) plasma (PPP) produces 3.92 +/- 1.6 mumol/L PPi compared with 2.85 +/- 0.7 mumol/L PPi in cartilage exposed to PPP alone. The platelet extract (PE) and %%%PDGF%%% are mitogenic for adult articular chondrocytes in high-density monolayer cultures. %%%Anti%%%-%%%PDGF%%% %%%antibodies%%% block the mitogenic effects of %%%PDGF%%% and PE. The uptake of thymidine labeled with tritium is 157% of control in cells exposed to PE, PPP, and polyclonal goat immunoglobulin G (IgG); 114% of control in cells exposed to PE, PPP, and %%%anti%%%-%%%PDGF%%% %%%antibody%%%; 148% of control in cells treated with %%%PDGF%%%, PPP, and goat IgG; and 98% of control in cells treated with %%%PDGF%%%, PPP, and %%%anti%%%-%%%PDGF%%% %%%antibody%%%. However, %%%anti%%%-%%%PDGF%%% %%%antibody%%% has no effect on PPi accumulation. PPi levels are 17.22 +/- 1.6 mumol/L in media from cartilage treated with PPP, goat IgG, and PE and 17.62 +/- 2.2 mumol/L in cartilage exposed to PE, PPP, and %%%anti%%%-%%%PDGF%%% %%%antibody%%%. We have further characterized the platelet factor responsible for the stimulation of PPi by cartilage. It is not mitogenic for chondrocytes, and it is not %%%PDGF%%%.

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...on the in vitro long-term growth of synoviocytes from patients with RA and rats with streptococcal cell wall (SCW) arthritis. Of the factors tested (%%%PDGF%%% , aFGF, bFGF, EGF, TGF-beta, IL-1-alpha, TNF-alpha and IFN-gamma), %%%PDGF%%%, was clearly the most potent stimulant of long-term growth of both rat and human synoviocytes. The strong mitogenic activity of rheumatoid synovial fluids was significantly inhibited by neutralizing %%%anti%%%-%%%PDGF%%% %%%antibody%%%, thus confirming the importance of %%%PDGF%%%. EGF, TGF-beta, IL-1-alpha, TNF-alpha, and IFN-gamma had minimal effects. Similar to the effects on anchorage-independent growth, TGF-beta 1 and 2, inhibited serum- or %%%PDGF%%% -stimulated anchorage-dependent growth. Considered in the context of other reports, these data support the view that cytokines such as %%%PDGF%%%, and possibly aFGF and bFGF, play major roles in stimulating synoviocyte hyperplasia in RA and SCW arthritis,

whereas TGF-beta may inhibit synoviocyte growth.

9/KWIC/16
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Platelet-derived growth factor (%%%PDGF%%%) is a potent mitogenic and chemotactic protein for a variety of cell types. Glomerular mesangial cells also respond to %%%PDGF%%% in terms of proliferation, but, to date, have not been examined for migratory behavior in response to a specific growth factor. Here, we examine the ability of isolated rat mesangial cells to migrate toward gradients of purified %%%PDGF%%%. Chemotaxis assays were performed in two-compartment blind well chambers, each compartment separated by a 14-microns porous filter membrane. Human %%%PDGF%%% was added to 200 microliters of RPMI 1640 medium in the lower compartment beneath the filters to make incremental concentrations from 2.5 to 50 units/ml. Control compartments received diluent without %%%PDGF%%% . Mesangial cells in RPMI 1640 medium were added to the upper compartments and the chambers were incubated for 8 hours at 37 degrees C. After...

... cells on the underside of the filter were counted by scanning electron microscopy. A linear dose response of mesangial cell migration toward increasing concentrations of %%%PDGF%%% was observed, achieving cell numbers of 9-fold over controls at 50 units/ml. Migratory cells were verified as mesangial cells by fluorescence expression of actin, myosin, and desmin and absence of expression of leukocyte common antigen and Ia antigen. Addition of equimolar concentrations of %%%PDGF%%% on both sides of the filter or addition of %%%anti%%%-%%%PDGF%%% %%%antibody%%% to the lower chamber containing %%%PDGF%%% negated the chemotactic response. These studies indicate that mesangial cells migrate in response to %%%PDGF%%%. This mechanism may, in part, play a role in some forms of mesangial proliferative glomerular disease.
; Cell Movement--Drug Effects--DE; Cells, Cultured; Dose-Response Relationship, Drug; Fluorescent %%%Antibody%%% Technique; Glomerular Mesangium--Metabolism--ME; Glomerular Mesangium--Ultrastructure--UL; Microscopy, Electron, Scanning; Microscopy, Fluorescence

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... that MCP-1 is the product of the gene JE, which was first recognized by its expression in fibroblasts stimulated with platelet-derived growth factor (%%%PDGF%%%). We therefore studied secretion of MCP-1 by three human fibroblast cell lines. Monocyte chemotactic activity was found in culture fluids of all three lines...

... for further study. Monocyte chemotactic activity secretion by confluent MRC-5 cultures continued after a switch to serum-free medium and was not inhibited by %%%anti%%%-%%%PDGF%%% %%%antibody%%% , indicating that secretion may not have been caused by autocrine release of %%%PDGF%%%. When concentrated serum-free MRC-5 culture fluid was injected into an HPLC gel filtration column, only one chemotactic activity peak was observed, which was...

... by an anti-MCP-1 affinity column, which indicates that all the chemotactic activity in MRC-5 culture fluid was accounted for by MCP-1. %%%PDGF%%% caused a marked increase in chemotactic activity over that found in serum-free culture fluid of MRC-5 or 501T cells. Immunoprecipitation by anti-human...

... showed two bands, corresponding to the two forms of MCP-1 previously described (MCP-1 alpha and beta); and the amounts increased in response to

%%%PDGF%%% stimulation. Thus, the reported increase in human fibroblast JE mRNA in response to %%%PDGF%%%-containing serum stimulation is reflected in increased secretion of the MCP-1 gene product.

9/KWIC/18

... J. Todaro, Proc. Natl. Acad. Sci. U.S.A. 81:4085-4089, 1984). In this study approximately 80% of the mitogenic activity was immunoprecipitated by %%%antibodies%%% raised against platelet-derived growth factor (%%%PDGF%%%). Immunoblotting indicated a true molecular size of 32 kDa for this %%%PDGF%%%-like growth factor. Analysis of poly(A)+ RNA from Neuro-2A cells demonstrated the expression of the c-sis oncogene in this cell line, whereas in vitro translation of the RNA yielded a 20-kDa protein recognized by %%%anti%%%-%%%PDGF%%% %%%antibodies%%% . Separation by reverse-phase high-pressure liquid chromatography demonstrated the presence of two distinct mitogenic activities in neuroblastoma-derived transforming growth factor preparations, one of which is antigenically related to %%%PDGF%%%. Both activities had the ability to induce anchorage-independent growth in normal rat kidney cells, both in the presence and in the absence of epidermal growth factor. It is concluded that Neuro-2A cells express c-sis with concomitant production and secretion of a %%%PDGF%%%-like growth factor, which plays a role in the induction of phenotypic transformation on normal rat kidney cells.

9/KWIC/19

The expression of platelet-derived growth factor (%%%PDGF%%%) receptors in porcine uterus and human skin in situ, was compared with that of cultured primary cells isolated from the same tissues. %%%PDGF%%% receptor expression was examined by monoclonal %%%antibodies%%% specific for the B type %%%PDGF%%% receptor and by RNA/RNA in situ hybridization with a probe constructed from a cDNA clone encoding the B type %%%PDGF%%% receptor. In porcine uterus tissue both mRNA and the protein product for the %%%PDGF%%% receptor were detected in the endometrium; the myometrium, in contrast, contained much lower amounts. Moreover, freshly isolated myometrial cells were devoid of %%%PDGF%%% receptors. However, after 1 d in culture receptors appeared, and after 2 wk of culturing essentially all of the myometrial cells stained positively with the %%%anti%%%-%%%PDGF%%% receptor %%%antibodies%%% and contained %%%PDGF%%% receptor mRNA. Similarly, B type %%%PDGF%%% receptors were not detected in normal human skin, but fibroblast-like cells from explant cultures of human skin possessed %%%PDGF%%% receptors. When determined by immunoblotting, porcine uterus myometrial membranes contained approximately 20% of the %%%PDGF%%% receptor antigen compared with the amount found in endometrial membranes. In addition, %%%PDGF%%% stimulated the phosphorylation of a 175-kD component, most likely representing autophosphorylation of the B type %%%PDGF%%% receptor in endometrial membranes, whereas only a marginal phosphorylation was seen in myometrial membranes. Taken together, these results demonstrate that %%%PDGF%%% receptor expression varies in normal tissues and that fibroblasts and smooth muscle cells do not uniformly express the receptor in situ. Furthermore, fibroblasts and smooth muscle cells that are released from tissues are induced to express %%%PDGF%%% receptors in response to cell culturing. The data suggest that, in addition to the availability of the ligand, %%%PDGF%%%-mediated cell growth in vivo is dependent on factors regulating expression of the receptor.
; %%%Antibodies%%%, Monoclonal--Diagnostic Use--DU; Cells, Cultured --Metabolism--ME; Fibroblasts--Cytology--CY; Immunoblotting; Immunohistoche mistry; Muscle, Smooth--Cytology--CY; Nucleic Acid Hybridization; Phosphorylation; Swine

Chemical Name: %%%Antibodies%%%, Monoclonal; (Receptors, Cell Surface; (Receptors, Platelet-Derived Growth Factor

9/KWIC/20

... in three simian sarcoma virus (SSV)-transformed cell lines with immunofluorescence and protein A-gold labeling techniques using rabbit polyclonal anti-platelet-derived-growth factor (%%%PDGF%%%) antisera. Antigenically reactive proteins were recognized in subcellular organelles related to protein synthesis and processing, including polyribosomes, endoplasmic reticulum, and the Golgi apparatus, as well...

... in isolated nuclei using Lowicryl K4M resin embedding techniques. Protein A-gold labeling was markedly reduced in sections of non-SSV-transformed fibroblasts incubated with %%%anti%%%-%%%PDGF%%% and absent from SSV-transformed cells if Epon resin was substituted for Lowicryl in the embedding process or if sections were with irrelevant antisera. Nuclear...

... protein synthesis and packaging but also may be found in the nucleus of SSV-transformed cells. These results raise the possibility that v-sis- or %%%PDGF%%%-like proteins may function within the nucleus of SSV-transformed cells.

; Cell Line; Cells, Cultured; Cytoplasm--Ultrastructure--UL; Fluorescent %%%Antibody%%% Technique; Mice; Microscopy, Electron; Platelet-Derived Growth Factor--Analysis--AN; Rats; Retroviridae Proteins--Analysis--AN

? ds

Set	Items	Description
S1	115	PDGF AND (ANTIBODIES OR ANTIBODY) AND CELL()PROLIF?
S2	73	S1 AND PY>1991
S3	42	S1 NOT S2
S4	28	S3 NOT PY=1991
S5	14	S3 AND PY=1991
S6	683	PDGF AND (ANTIBODIES OR ANTIBODY) NOT S1
S7	431	S6 AND PY>1991
S8	252	S6 NOT S7
S9	40	S8 AND ANTI()PDGF

? t s9/kwic/21-30

9/KWIC/21

U-1810, a human large-cell lung cancer line, was found to express a %%%PDGF%%% -like growth factor. 35S-cysteine labelling and immunoprecipitation revealed the synthesis and secretion of a 31-kDa %%%PDGF%%%-like protein. Serum-free conditioned medium contained %%%PDGF%%% -receptor-competing and mitogenic activity when tested on human fibroblasts. Whereas the receptor-competing activity was fully neutralized by %%%anti%%%-%%%PDGF%%% %%%antibodies%%%, the mitogenic activity was only partially affected. We therefore probed U-1810 mRNA with a panel of growth-factor DNA clones. We found expression of the genes for %%%PDGF%%% A- and B-chains, TGF-alpha, TGF-beta and IGF-II but not EGF or IGF-I. U-1810 cells lacked specific binding sites for %%%PDGF%%% but showed specific binding of EGF and expressed EGF-receptor transcripts. Thus, U-1810 is an example of a human tumor cell line that expresses...

9/KWIC/22

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Human melanoma cell lines of primary and metastatic origin express the genes encoding the chains of platelet-derived growth factor (%%%PDGF%%%) and produce a %%%PDGF%%%-like growth factor.

Normal human melanocytes and five human melanoma cell lines were analyzed for production of platelet-derived growth factor (%%%PDGF%%%)-like activity. Three of the melanoma cell lines released an activity that inhibited binding of 125I-labeled %%%PDGF%%% to human foreskin fibroblasts and stimulated [3H]thymidine incorporation in such cells. These activities were inhibited by the addition of %%%anti%%%-%%%PDGF%%% %%%antibodies%%%. All three factor-producing cell lines were derived from the same patient--one originated from the primary tumor (WM 115), and two were from individual...

... was purified to homogeneity. Analysis by reverse-phase high-pressure liquid chromatography of reduced and alkylated factor revealed an elution pattern identical to that of %%%PDGF%%% A chains. Thus, the native molecule appears to be a homodimer of %%%PDGF%%% A chains. Blot-hybridization analysis of poly(A)+ RNA from the cell lines with 32P-labeled %%%PDGF%%% A chain and B chain (SIS product) cDNA probes revealed a relative abundance of B chain transcripts in the cell line originating from the primary...
...only but expression of A chain in all three cell lines. We conclude that the two structural genes encoding each of the subunit chains of %%%PDGF%%% can be expressed in human melanoma cells and that the two genes can be independently expressed in such cells.

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%%%Antibodies%%% against platelet-derived growth factor inhibit acute transformation by simian sarcoma virus.

... the molecular mechanism of neoplastic transformation was provided by the finding of a near identity in amino-acid sequence between the platelet-derived growth factor (%%%PDGF%%%) B-chain and a region in the transforming protein, p28sis, of simian sarcoma virus (SSV), an agent that causes sarcomas and gliomas in experimental animals...

... between the molecular biology of normal mitogenesis and oncogenesis since it suggests that the transforming activity of SSV is caused by a growth factor. Although %%%PDGF%%% agonist activity has been isolated from conditioned medium of SSV-transformed cells, it is not clear whether infection of responsive cells by SSV leads solely to autocrine stimulation of growth by a secreted %%%PDGF%%%-like factor or whether other, possibly intracellular, activities of p28sis or its processed products contribute to the transformation. To distinguish between these possibilities, we have studied the effect of %%%anti%%%-%%%PDGF%%% %%%antibodies%%% on acute SSV-transformation, and report here that these %%%antibodies%%% inhibit both proliferation and SSV-induced morphological changes in human diploid fibroblasts.

Descriptors: %%%Antibodies%%%; *Cell Transformation, Neoplastic--Drug Effects--DE; *Cell Transformation, Viral--Drug Effects--DE; *Platelet-Derived Growth Factor--Immunology--IM; *Retroviridae --Pathogenicity--PY; *Sarcoma Viruses, Simian--Pathogenicity...

Chemical Name: %%%Antibodies%%%; (Peptides; (Platelet-Derived Growth Factor; (Transforming Growth Factors

9/KWIC/24
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Visualization of platelet-derived growth factor (%%%PDGF%%%) and

%%%PDGF%%% -like growth factors in cultured cells has been achieved by cryo-ultramicrotomy in combination with immunogold labeling. Immunogold staining of cryosections requires a mild chemical fixation in order to ensure preservation of antigenicity and ultrastructural details. Therefore the effect of several chemical fixatives on the antigenic properties of %%%PDGF%%% and %%%PDGF%%% -like growth factors was studied by indirect immunofluorescence using a polyclonal %%%anti%%%-%%%PDGF%%% antiserum. These studies demonstrated that formaldehyde has no effect on antigenicity, in contrast to glutaraldehyde or acrolein. For this reason formaldehyde was used as the only fixative for the visualization of %%%PDGF%%% in cryosections. %%%PDGF%%% was visualized in cryosections of normal human fibroblasts, preincubated with %%%PDGF%%% under various conditions. Preincubation at 4 degrees C with %%%PDGF%%% resulted in partial internalization of the growth factor. During subsequent warming of the cells to 37 degrees C %%%PDGF%%% was translocated to the nucleus. %%%PDGF%%% was also detected in the cytoplasm of tumor cells producing endogenous %%%PDGF%%%-like growth factors (neuroblastoma and simian sarcoma virus-transformed cells) but in these cases no significant amounts of these growth factors were present in the nucleus or at the extracellular surface of these cells. These results will be discussed in view of the intracellular routing of %%%PDGF%%% in normal responsive cells and of %%%PDGF%%%-like growth factors in factor-producing cells.

; Acrolein; Cell Line; Cell Line, Transformed; Detergents; Fibroblasts; Fixatives; Fluorescent %%%Antibody%%% Technique; Formaldehyde; Frozen Sections; Glutaral; Immunohistochemistry; Microscopy, Electron; Microtomy; Neuroblastoma; Polyethylene Glycols; Tumor Cells, Cultured

9/KWIC/25

... the day of birth, and new oligodendrocytes continue to develop over several weeks, just as in vivo. Here we show that platelet-derived growth factor (%%%PDGF%%%) can replace type-1-astrocyte-conditioned medium in restoring the normal timing of oligodendrocyte differentiation in vitro and that %%%anti%%%-%%%PDGF%%% %%%antibodies%%% inhibit this property of the appropriately conditioned medium. We also show that %%%PDGF%%% is present in the developing optic nerve. These findings suggest that type-1-astrocyte-derived %%%PDGF%%% drives the clock that times oligodendrocyte development.

9/KWIC/26

... molecular weight (MW) of 25 kDa estimated by gel permeation chromatography. GDGF-1 activity was neutralized by a goat anti-human platelet derived growth factor (%%%PDGF%%%) %%%antibody%%%, indicating that the two factors were immunologically related. Furthermore, U-251 Mg cells constitutively expressed c-sis mRNA. When U-251 Mg cells were stimulated with bacterial lipopolysaccharide, 2 novel growth factors (GDGF-2 and GDGF-3) were produced in addition to the %%%PDGF%%%-like substance. GDGF-2 was determined to be greater than 100 kDa MW and was not neutralized by the goat %%%anti%%%-%%%PDGF%%% antiserum. The biological activity of GDGF-3 was also heat- and acid-resistant with an apparent 14 kDa MW. This factor also did not show any common antigenicity with %%%PDGF%%%. GDGF-2 and GDGF-3 are currently under investigation and evidence as to their natures will be published elsewhere. Our findings with this glioma cell...

9/KWIC/27

Platelet-derived growth factor (%%%PDGF%%%) has been implicated in several nonmalignant pathophysiological processes, including proliferative diseases of the kidney. Glomerular mesangial cells secrete a %%%PDGF%%% -like factor and express the %%%PDGF%%% A-chain and c-sis (or B-chain) mRNAs. We report here that both mRNAs are induced by serum and this effect can be mimicked by recombinant %%%PDGF%%%, which also markedly stimulates DNA synthesis. Other growth factors, such as epidermal growth factor (EGF), transforming growth factor type alpha, basic fibroblast growth factor (bFGF), and tumor necrosis factor type alpha (TNF-alpha) also are mitogenic for human mesangial cells and induce expression of the %%%PDGF%%% mRNAs. EGF, TNF-alpha, and bFGF also stimulate these cells to secrete a %%%PDGF%%% -like factor. Furthermore, %%%anti%%%-%%%PDGF%%% %%%antibody%%% partially abrogates the mitogenic effect of EGF, suggesting that mitogen-stimulated %%%PDGF%%% synthesis in mesangial cells is at least partly responsible for cell growth induced by other growth factors. In contrast to these results, transforming growth factor...

... on message levels can be dissociated from DNA synthesis. These data suggest that several peptide growth factors regulate the growth of mesangial cells and that %%%PDGF%%% may be an effector molecule that plays a role in the mitogenic response to many of these growth stimuli.

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Autoregulation of MeWo metastatic melanoma cell growth: characterization of intracellular (FGF, MGSA) and secreted (%%%PDGF%%%) growth factors.

... fibroblasts (CCL39, NRK-49F, NIH-3T3) but not in BHK-21 kidney cells. This activity appears to be closely related to platelet-derived growth factor (%%%PDGF%%%) based on 1) its cationic nature, heat and acid resistance, but sensitivity to reducing agents; 2) its apparent molecular weight (33 kDaltons) as estimated by Biogel filtration, once dissociated from binding proteins by mild acidic treatment; 3) its weak affinity for heparin; and 4) its ability to compete with 125I-%%%PDGF%%% for binding to human and rodent fibroblasts, and to be recognized by %%%anti%%%-%%%PDGF%%% %%%antibodies%%%. Although MeWo cells coexpress the %%%PDGF%%%-A and %%%PDGF%%% -B (c-sis) chain gene transcripts, the secreted product shows reactivity on CCL39 fibroblasts more compatible with the %%%PDGF%%%-BB than with the %%%PDGF%%%-AB isoform. MeWo cell lysates contain activities that bind moderately and strongly to heparin-Sepharose, being eluted with 1.0 and 2.0 M NaCl...

... not been fully characterized and is probably not the product of the acidic FGF gene. In addition, MeWo cells react positively with the FB2 AH7 %%%antibody%%% , thus indicating that they elaborate material similar to melanoma growth-stimulating activity (MGSA). MeWo cells proliferate in serum-free medium in a cell-density-dependent fashion, both in liquid and semisolid cultures. Their division is modestly enhanced by basic FGF and by human and porcine %%%PDGF%%% but not by the factors that they release. However, the absence of demonstrable 125I-%%%PDGF%%% binding sites on MeWo cells, in conjunction with their lack of sensitivity to suramin growth inhibition, suggests that the secreted %%%PDGF%%% does not act as an autocrine factor. Instead, the autonomous proliferation of MeWo melanoma cells may result from the concerted action of basic FGF and...

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... fibroblasts competent to initiate DNA synthesis in vitro in the presence of platelet-poor plasma. This biological activity resembles that of platelet-derived growth factor (%%%PDGF%%%). After separation from

putative associated binding proteins by chromatography under acidic conditions, the macrophage-derived factor exhibited a relative molecular weight similar to that of highly purified human %%%PDGF%%%. The factor bound to a monospecific %%%antibody%%% to human %%%PDGF%%% and thus could be quantitated in an enzyme immunoassay for %%%PDGF%%%. It competed with radiolabeled human %%%PDGF%%% for receptor sites for %%%PDGF%%% on rat lung fibroblasts, and binding to these receptor sites could be specifically inhibited by %%%anti%%%-%%%PDGF%%% . These data strongly support the view that the factor derived from rat alveolar macrophages is homologous to human %%%PDGF%%% and is similar to human macrophage-derived %%%PDGF%%%-like growth factor. Furthermore, we have demonstrated that the lung contains both an effector cell (pulmonary macrophage) and a potential target cell (interstitial fibroblast) for this cytokine. Therefore the rat appears to be an appropriate animal model in which to study macrophage-derived %%%PDGF%%% -like growth factors as mediators of proliferation in pulmonary fibrogenesis.

9/KWIC/30

One of the earliest effects of platelet-derived growth factor (%%%PDGF%%%) on human fibroblasts in culture is an induction of membrane ruffling. The morphology of the ruffles induced by %%%PDGF%%% is unique in that they form circular arrangements on the dorsal side of the cells. Here we report that the induction of circular ruffle arrangements is an effect specific for %%%PDGF%%%, dose-dependent and inhibitable by %%%anti%%%-%%%PDGF%%% %%%antibodies%%% . We have attempted to utilize this effect to design a rapid and sensitive bioassay for %%%PDGF%%%. The "membrane ruffling assay" is compared with other methods to measure %%%PDGF%%% and its specificity with regard to the different dimeric forms of %%%PDGF%%% is discussed. Introduction of Ca2+ into the cells via the Ca2+ ionophore A23187 or the addition of the tumor-promor 12-O-tetradecanoylphorbol-13-acetate...

...induce circular ruffle formations on human fibroblasts, neither does the addition of the combination of these two agents. However, addition of TPA almost completely inhibits %%%PDGF%%%-induced circular ruffle formations. Further, we find a shift in the time-course of the %%%PDGF%%%-induced circular ruffle formations by sodium orthovanadate, an inhibitor of protein tyrosine phosphatases. This may indicate the involvement of protein phosphorylation in the regulation of %%%PDGF%%%-induced membrane ruffling.
? t s9/kwic/31-40

9/KWIC/31

... control medium. Part of this activity was due to molecules that resemble a mitogen first isolated from platelets and known as platelet-derived growth factor (%%%PDGF%%%), since these cells released %%%PDGF%%% measured in a radioreceptor assay (355 +/- 117 pg per milliliter per 48 hours; n = 6) and since %%%anti%%%-%%%PDGF%%% %%%antibody%%% neutralized 38 +/- 7 percent of this mitogenic activity (range, 13 to 60 percent; n = 6 carotid-plaque isolates). Two human genes encode distinct %%%PDGF%%% subunits that form dimers in different combinations to create biologically active %%%PDGF%%% . Cells cultured from human atheroma contained mRNAs for the %%%PDGF%%% A chain (16 of 17 isolates) but none (of 13) that encoded %%%PDGF%%% B chain (the c-sis proto-oncogene product). We conclude that smooth-muscle cells from diseased human arteries can secrete mitogenic activity, some of which resembles %%%PDGF%%%, and that these cells express the gene for the %%%PDGF%%% A chain selectively. This capacity to produce an endogenous, potentially self-stimulatory (autocrine) growth factor may help to explain how replication of smooth-muscle cells...

9/KWIC/32
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...rat aortas. Old SMCs grew more rapidly than young SMCs in the presence of medium containing competence factors (10% FCS or platelet-derived growth factor [%%%PDGF%%%]) as well as in their absence (2% PDS or serum-free media) as determined both by a short-term thymidine incorporation assay and by cell counts. Lysates prepared from old SMCs that had been grown in the absence of serum or %%%PDGF%%% stimulated proliferation of target cells more than lysates prepared from young SMCs; the effect was inversely related to cell density of the SMCs. This stimulatory effect of lysates was completely blocked by %%%antibody%%% to %%%PDGF%%% . After the growth-promoting activity of lysates was eliminated by %%%anti%%%-%%%PDGF%%% , growth-inhibiting activity was revealed. Lysates prepared from old SMCs had significantly less capacity to inhibit target cell growth. In the presence of exogenous heparin both the serum- or %%%PDGF%%%-stimulated proliferation and serum-free proliferation of old SMCs were decreased to the level of proliferation of young SMCs. These results suggest that the balance...

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We examined the effect of highly purified platelet-derived growth factor (%%%PDGF%%%) on prostacyclin (PGI2) release by cultured human umbilical vein and bovine aortic endothelial cells. %%%PDGF%%% tested at concentrations equal to or exceeding those observed in serum did not increase endothelial cell PGI2 synthesis as measured by radioimmunoassay of its metabolite, 6-keto-PGF1 alpha. In contrast, cells incubated with 20% human whole blood serum (WBS) demonstrated significantly increased PGI2 production (fivefold stimulation). Addition of %%%anti%%%-%%%PDGF%%% %%%antibody%%% to the 20% WBS did not attenuate the increased synthesis of PGI2. Incubation with 20% plasma-derived serum (PDS) that was deficient in %%%PDGF%%% produced stimulation of PGI2 release similar to 20% WBS. These results demonstrate that %%%PDGF%%% does not cause increased PGI2 synthesis in cultured human endothelial cells of human or bovine origin, and further suggest that the stimulation observed with serum...

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J774A.1 macrophage cell line produces %%%PDGF%%%-like and non-%%%PDGF%%% -like growth factors for bone cells.
... secrete growth-promoting activities which have an affinity for heparin. The first partially purified material, termed HEP I, appears to contain platelet-derived growth factor (%%%PDGF%%%)-like activity. It has a molecular weight of about 30,000 daltons, inhibits the binding of labeled %%%PDGF%%% to its receptors, reacts with polyclonal anti-human %%%PDGF%%% %%%antibody%%% , and exhibits mitogenic activity for osteoblasts, which is partially blocked by %%%anti%%%-%%%PDGF%%% antisera. Like %%%PDGF%%%, HEP I is active in a wide variety of mesenchyme-derived cells, including osteoblasts, chondrocytes, smooth muscle cells, fibroblasts, 3T3 cells and NRK cells. The...

... cells contain mRNA, which hybridizes to a v-sis DNA probe, suggesting that they express the c-sis gene, which contains the code for a %%%PDGF%%% -like protein. The second factor, HEP II, has an approximate molecular weight of 20,000 daltons and possesses substantial mitogenic activity for osteoblasts, chondrocytes, and...

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... a 4.2-kilobase mRNA complementary to the c-sis gene, a proto-oncogene coding for one of the chains of platelet-derived growth factor (%%%PDGF%%%). Concomitantly, these cells released a mediator with the properties of %%%PDGF%%% , including: chemotactic factor for smooth muscle cells whose activity was resistant to heat and acid, but sensitive to reduction; mitogenic (competence) activity for fibroblasts; ability to compete with %%%PDGF%%% for its receptor; and precipitated by an %%%anti%%%-%%%PDGF%%% %%%antibody%%% . While blood monocytes did not contain c-sis mRNA transcripts, monocytes matured in vitro expressed c-sis, consistent with the concept that expression of c-sis occurs during the differentiation of monocytes into alveolar macrophages. Together with the known actions of %%%PDGF%%% , these observations suggest that the c-sis proto-oncogene and its %%%PDGF%%% product are part of the armamentarium available to the alveolar macrophages for normal lung defense and participation in lung inflammation.

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Activated human monocytes express the c-sis proto-oncogene and release a mediator showing %%%PDGF%%%-like activity.
... mediator that attracts smooth muscle cells and cooperates with other mediators to stimulate fibroblast proliferation. This mediator is very similar to platelet-derived growth factor (%%%PDGF%%%): its chromatographic properties and chemical stability are similar to those of %%%PDGF%%%, it competes with 125I-%%%PDGF%%% for binding to fibroblasts and it immunoprecipitates with %%%anti%%%-%%%PDGF%%% %%%antibodies%%% . In parallel, stimulated monocytes, but not resting monocytes, express the c-sis proto-oncogene, a gene coding for one of the %%%PDGF%%% chains, consistent with the concept that expression of the c-sis proto-oncogene may be involved in the ability of mononuclear phagocytes to modulate the...

9/KWIC/37
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... and exhibited marked size and charge heterogeneity when subjected to gel chromatographies. GSA differed from many other known growth factors, mainly platelet derived growth factor (%%%PDGF%%%), through the behavior on ion exchange chromatography, the heat sensitivity and the lack of decline in activity in the presence of %%%anti%%% %%%PDGF%%% %%%antibodies%%%. The data suggests that several growth stimulating proteins can be obtained through the lysis of SMC or fibroblasts with possible implications for atherosclerosis and wound...
; %%%Antibodies%%%--Physiology--PH; Cattle; Cell Division; Cells, Cultured; Chromatography, Gel; Chromatography, Ion Exchange; DNA --Biosynthesis--BI; Fibroblasts--Metabolism--ME; Growth Substances --Isolation and Purification--IP; Heat...
Chemical Name: Trypsin; (%%%Antibodies%%%; (Growth Substances; (Platelet-Derived Growth Factor; (Protease Inhibitors; (Thymidine; (DNA

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... 343 MGa Cl 2, cultured under serum-free conditions, was found to release a factor that competed with 125I-labeled platelet-derived growth

factor (125I-%%%PDGF%%%) for binding to human foreskin fibroblasts. The concentration of competing activity in conditioned medium was equal to 20-30 ng of %%%PDGF%%% per ml. The %%%PDGF%%% receptor competing activity had an elution position on Sephadex G-200 close to that of tracer %%%PDGF%%% . The same fractions in the chromatogram also contained growth-promoting activity and material active in a %%%PDGF%%% radioimmunoassay. Incubation of partially purified, 125I-labeled glioma factor with fibroblasts, or rabbit %%%anti%%%-%%%PDGF%%% serum, led to the selective binding of a component with an estimated Mr of 31,000, as shown by NaDodSO4/gel electrophoresis under nonreducing conditions. After reduction this component migrated as a Mr 18,000 protein. Thus, the behavior in NaDodSO4/gel electrophoresis was similar to that of %%%PDGF%%%. Furthermore, incubation of partially purified glioma factor with immobilized %%%PDGF%%% %%%antibodies%%% markedly decreased the amount of %%%PDGF%%% receptor competing activity remaining in the supernatant. These results suggest that the factor produced by glioma cells has structural, immunological, and functional resemblance to %%%PDGF%%%. We previously reported that a human osteosarcoma cell line produces a %%%PDGF%%%-like molecule with growth-promoting activity. Taken together with the recent finding that %%%PDGF%%% is homologous to the transforming gene product of simian sarcoma virus, our present data give additional support for the idea that an autocrine activation of the %%%PDGF%%% receptor may be operational in the growth of human tumors of mesenchymal or glial origin.

9/KWIC/39

The platelet-derived growth factor (%%%PDGF%%%) is the principal mitogen in serum for cultured cells of mesenchymal origin. %%%PDGF%%% also is a potent chemotactic protein for inflammatory cells and for cells required for wound repair. Because activity levels of %%%PDGF%%% in biological fluids are difficult to measure, we attempted to develop a radioimmunoassay for %%%PDGF%%%. Rabbits were immunized with purified %%%PDGF%%%; the antiserum obtained was monospecific for %%%PDGF%%% in immunodiffusion analysis against concentrated platelet lysates, serum, and plasma. A radioimmunoassay for %%%PDGF%%% was developed with a sensitivity of congruent to 0.2 ng/ml. Levels of %%%PDGF%%% in plasma/serum were measured and compared with %%%PDGF%%% levels determined by a receptor-competition assay and by a standard biological assay measuring incorporation of [3H]thymidine into 3T3 cells. Radioimmunoassay showed apparent %%%PDGF%%% levels of 50 ng/ml in human plasma and 103 ng/ml in serum. The 50 ng/ml %%%PDGF%%% in plasma was unexpected because the plasma samples contained little or no platelet release products as determined by very low levels of platelet factor 4. We therefore sought an immunologically reactive %%%PDGF%%% molecule in human plasma. No immunologically reactive protein was detected by immunodiffusion analysis or when plasma was treated with an immunoaffinity gel. Subsequently, a 125I-%%%PDGF%%%-binding protein was identified; the 125I-%%%PDGF%%% -plasma-binding protein complex was not reactive with %%%anti%%%-%%%PDGF%%% immunoglobulin. Correction for 125I-%%%PDGF%%% bound by the plasma-binding protein established serum levels of %%%PDGF%%% of congruent to 50 ng/ml; congruent to 50 ng/ml %%%PDGF%%% was found in serum by radioreceptor-competition assays and by mitogenic assays as well. The plasma-binding protein may serve to clear %%%PDGF%%% released in the circulation, thereby limiting %%%PDGF%%% activity to its local interactions at the site of blood-vessel injury.
; %%%Antibody%%% Specificity; Blood Proteins--Isolation and Purification --IP; Growth Substances--Immunology--IM; Mice; Peptides--Immunology--IM; Protein Binding; Rabbits

9/KWIC/40

Quiescent BALB/c-3T3 cells exposed briefly to platelet-derived growth factor (%%%PDGF%%%) become "competent" to replicate their DNA even if %%%PDGF%%% is removed from cell culture medium prior to the onset of DNA synthesis. We have suggested that persistence of the %%%PDGF%%%-induced competent state reflects a rapidly induced and relatively stable biochemical change within the target cells. Others suggest that the phenomenon reflects a long-term association between %%%PDGF%%% and its target cells or perhaps between %%%PDGF%%% and the cell culture dish. This controversy has been addressed (a) by examining the effect of %%%anti%%%-%%%PDGF%%% %%%antibodies%%% on %%%PDGF%%% -induced competence and (b) by studying the chemical fate of 125I-labeled %%%PDGF%%%. %%%Anti%%%-%%%PDGF%%% %%%antibodies%%% inactive both soluble and surface-bound %%%PDGF%%%. However, if quiescent 3T3 cells are exposed to %%%PDGF%%% for as little as 30 min, subsequent addition of these %%%antibodies%%% to the culture medium does not prevent the mitogenic response. Under conditions where the %%%PDGF%%%-induced competent state decays stochastically with a t1/2 of 18-20 h, cell-associated 125I-%%%PDGF%%% decays with a t1/2 of approximately 50 min. These data do not support the concept that persistence of the %%%PDGF%%%-induced competent state reflects a long-term association between %%%PDGF%%% and the target cells or between %%%PDGF%%% and the culture dish.
; %%%Antibodies%%%; Cell Division--Drug Effects--DE; Fibroblasts--Drug Effects--DE; Growth; Growth Substances--Immunology--IM; Mice; Mice, Inbred BALB C; Peptides--Immunology--IM; Time Factors
Chemical Name: %%%Antibodies%%%; (Growth Substances; (Peptides; (Platelet-Derived Growth Factor
? t s9/3,ab/3,5,15,16,22,39

9/3,AB/3
DIALOG(R)File 155:MEDLINE(R)

07050111 91266260
Stimulation of growth of human breast cancer cells (T47D) by platelet derived growth factor [published erratum appears in Cancer Lett 1991 Sep;59(3):267]
Ginsburg E; Vonderhaar BK
Laboratory of Tumor Immunology and Biology, National Cancer Institute, Bethesda, MD 20892.
Cancer Lett (NETHERLANDS) Jun 14 1991, 58 (1-2) p137-44, ISSN 0304-3835 Journal Code: CMX
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The human breast cancer cell lines T47D and MCF-7, respond to the mitogenic action of exogenously added %%%PDGF%%% with a 2-3-fold increase in cell number. The maximal response was obtained at a concentration of 1.25 half maximal units/ml (125 ng/ml). %%%PDGF%%% -AA was even more effective than %%%PDGF%%%-AB while %%%PDGF%%%-BB was without effect. The growth-enhancing activity of %%%PDGF%%% was completely abolished by Fab fragments of %%%anti%%% %%%PDGF%%%. Within 7 min of addition of %%%PDGF%%% to cultures of T47D cells, specific phosphorylation of a 65-kDa protein was observed. T47D cells contain specific receptors for %%%PDGF%%% with approximately 4-7 x 10(4) sites (kDa of 3-4 x 10(-10) M) per cell.

9/3,AB/5
DIALOG(R)File 155:MEDLINE(R)

07048075 91218086
Production of platelet derived growth factor B chain (%%%PDGF%%%-B/c-sis)

mRNA and immunoreactive %%%PDGF%%% B-like polypeptide by rheumatoid synovium: coexpression with heparin binding acidic fibroblast growth factor-1.

Remmers EF; Sano H; Lafyatis R; Case JP; Kumkumian GK; Hla T; Maciag T; Wilder RL

Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD 20892.

J Rheumatol (CANADA) Jan 1991, 18 (1) p7-13, ISSN 0315-162X
Journal Code: JWX

Languages: ENGLISH

Document type: JOURNAL ARTICLE

We present evidence supporting the hypothesis that locally produced platelet derived growth factor (%%%PDGF%%%) B-like polypeptides, as well as heparin binding growth factor-1 (HBGF-1), are involved in stimulating the pronounced hyperplasia of rheumatoid synovial stromal fibroblastlike cells. Explanted rheumatoid synovial tissues in vitro spontaneously secreted, in a time dependent manner, mitogenic activity for rheumatoid synoviocytes that was neutralizable by %%%anti%%%-%%%PDGF%%% %%%antibody%%%. %%%PDGF%%% B/c-sis mRNA transcripts were detected in synovium from patients with rheumatoid arthritis (RA) (n = 5). Spontaneous %%%PDGF%%% B-like synthesis was detected by immunoprecipitation of radiolabeled %%%PDGF%%% B-like polypeptides secreted by explanted tissues. Furthermore, rheumatoid synovial tissues, particularly macrophage-like cells, immunostained specifically with %%%anti%%%-%%%PDGF%%% B chain. The extent and intensity of staining and mononuclear cell infiltration were highly correlated. Immunostaining of osteoarthritic and normal synovial tissues was significantly less than RA synovium. %%%PDGF%%% -B immunostaining of synovial specimens previously characterized for expression of HBGF-1, the precursor of acidic fibroblast growth factor (aFGF), revealed that the extent and intensity of expression of HBGF-1 and %%%PDGF%%%-B were highly correlated.

9/3,AB/15
DIALOG(R)File 155:MEDLINE(R)

06463790 90253810

Cytokines and growth regulation of synoviocytes from patients with rheumatoid arthritis and rats with streptococcal cell wall arthritis.

Remmers EF; Lafyatis R; Kumkumian GK; Case JP; Roberts AB; Sporn MB; Wilder RL

Arthritis and Rheumatism Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland 20892.

Growth Factors (SWITZERLAND) 1990, 2 (2-3) p179-88, ISSN 0897-7194
Journal Code: AOI

Languages: ENGLISH

Document type: JOURNAL ARTICLE

Paracrine growth factors probably stimulate the pathologic proliferation of synovial fibroblast-like cells (synoviocytes) in rheumatoid arthritis (RA), but the relative importance of various factors is highly controversial. To address this problem, we compared the effects of highly purified or recombinant cytokines, in serum-free medium, on the in vitro long-term growth of synoviocytes from patients with RA and rats with streptococcal cell wall (SCW) arthritis. Of the factors tested (%%%PDGF%%%, aFGF, bFGF, EGF, TGF-beta, IL-1-alpha, TNF-alpha and IFN-gamma), %%%PDGF%%% , was clearly the most potent stimulant of long-term growth of both rat and human synoviocytes. The strong mitogenic activity of rheumatoid synovial fluids was significantly inhibited by neutralizing %%%anti%%%-%%%PDGF%%% %%%antibody%%%, thus confirming the importance of %%%PDGF%%% . EGF, TGF-beta, IL-1-alpha, TNF-alpha, and IFN-gamma had minimal effects. Similar

to the effects on anchorage-independent growth, TGF-beta 1 and 2, inhibited serum- or %%%PDGF%%%-stimulated anchorage-dependent growth. Considered in the context of other reports, these data support the view that cytokines such as %%%PDGF%%% , and possibly aFGF and bFGF, play major roles in stimulating synoviocyte hyperplasia in RA and SCW arthritis, whereas TGF-beta may inhibit synoviocyte growth.

9/3,AB/16
DIALOG(R)File 155:MEDLINE(R)

06456295 90189784
Glomerular mesangial cell migration in response to platelet-derived growth factor.
Barnes JL; Hevey KA
Department of Pathology, Rhode Island Hospital, Providence.
Lab Invest (UNITED STATES) Mar 1990, 62 (3) p379-82, ISSN 0023-6837
Journal Code: KZ4
Contract/Grant No.: AM-30393, AM, NIADDK; DK-38758, DK, NIDDK
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Platelet-derived growth factor (%%%PDGF%%%) is a potent mitogenic and chemotactic protein for a variety of cell types. Glomerular mesangial cells also respond to %%%PDGF%%% in terms of proliferation, but, to date, have not been examined for migratory behavior in response to a specific growth factor. Here, we examine the ability of isolated rat mesangial cells to migrate toward gradients of purified %%%PDGF%%%. Chemotaxis assays were performed in two-compartment blind well chambers, each compartment separated by a 14-microns porous filter membrane. Human %%%PDGF%%% was added to 200 microliters of RPMI 1640 medium in the lower compartment beneath the filters to make incremental concentrations from 2.5 to 50 units/ml. Control compartments received diluent without %%%PDGF%%% . Mesangial cells in RPMI 1640 medium were added to the upper compartments and the chambers were incubated for 8 hours at 37 degrees C. After fixation, the number of cells on the underside of the filter were counted by scanning electron microscopy. A linear dose response of mesangial cell migration toward increasing concentrations of %%%PDGF%%% was observed, achieving cell numbers of 9-fold over controls at 50 units/ml. Migratory cells were verified as mesangial cells by fluorescence expression of actin, myosin, and desmin and absence of expression of leukocyte common antigen and Ia antigen. Addition of equimolar concentrations of %%%PDGF%%% on both sides of the filter or addition of %%%anti%%%-%%%PDGF%%% %%%antibody%%% to the lower chamber containing %%%PDGF%%% negated the chemotactic response. These studies indicate that mesangial cells migrate in response to %%%PDGF%%% . This mechanism may, in part, play a role in some forms of mesangial proliferative glomerular disease.

9/3,AB/22
DIALOG(R)File 155:MEDLINE(R)

06211558 87016914
Human melanoma cell lines of primary and metastatic origin express the genes encoding the chains of platelet-derived growth factor (%%%PDGF%%%) and produce a %%%PDGF%%%-like growth factor.
Westermark B; Johnsson A; Paulsson Y; Betsholtz C; Heldin CH; Herlyn M; Rodeck U; Koprowski H
Proc Natl Acad Sci U S A (UNITED STATES) Oct 1986, 83 (19) p7197-200, ISSN 0027-8424 Journal Code: PV3
Contract/Grant No.: CA-25874, CA, NCI; CA-21124, CA, NCI; CA-10815, CA, NCI

Languages: ENGLISH
Document type: JOURNAL ARTICLE
Normal human melanocytes and five human melanoma cell lines were analyzed for production of platelet-derived growth factor (%%%PDGF%%%)-like activity. Three of the melanoma cell lines released an activity that inhibited binding of 125I-labeled %%%PDGF%%% to human foreskin fibroblasts and stimulated [3H]thymidine incorporation in such cells. These activities were inhibited by the addition of %%%anti%%%-%%%PDGF%%% %%%antibodies%%%. All three factor-producing cell lines were derived from the same patient--one originated from the primary tumor (WM 115), and two were from individual lymph-node metastases (WM 239A and WM 266-4). The factor produced by WM 266-4 cells was characterized biochemically in detail. Immunoprecipitated, the metabolically labeled factor migrated in NaDod-SO4/gel electrophoresis as a homogeneous Mr 31,000 species, which under reducing conditions was resolved into two species of Mr 16,500 and Mr 17,000, implying a dimeric structure of the molecule. The factor was purified to homogeneity. Analysis by reverse-phase high-pressure liquid chromatography of reduced and alkylated factor revealed an elution pattern identical to that of %%%PDGF%%% A chains. Thus, the native molecule appears to be a homodimer of %%%PDGF%%% A chains. Blot-hybridization analysis of poly(A)+ RNA from the cell lines with 32P-labeled %%%PDGF%%% A chain and B chain (SIS product) cDNA probes revealed a relative abundance of B chain transcripts in the cell line originating from the primary tumor tissue only but expression of A chain in all three cell lines. We conclude that the two structural genes encoding each of the subunit chains of %%%PDGF%%% can be expressed in human melanoma cells and that the two genes can be independently expressed in such cells.

9/3,AB/39
DIALOG(R)File 155:MEDLINE(R)

03967271 83291249
Human platelet-derived growth factor: radioimmunoassay and discovery of a specific plasma-binding protein.
Huang JS; Huang SS; Deuel TF
J Cell Biol (UNITED STATES) Aug 1983, 97 (2) p383-8, ISSN 0021-9525
Journal Code: HMV
Contract/Grant No.: CA22409, CA, NCI; HL14147, HL, NHLBI; T32-HL07088, HL, NHLBI
Languages: ENGLISH
Document type: JOURNAL ARTICLE
The platelet-derived growth factor (%%%PDGF%%%) is the principal mitogen in serum for cultured cells of mesenchymal origin. %%%PDGF%%% also is a potent chemotactic protein for inflammatory cells and for cells required for wound repair. Because activity levels of %%%PDGF%%% in biological fluids are difficult to measure, we attempted to develop a radioimmunoassay for %%%PDGF%%%. Rabbits were immunized with purified %%%PDGF%%%; the antiserum obtained was monospecific for %%%PDGF%%% in immunodiffusion analysis against concentrated platelet lysates, serum, and plasma. A radioimmunoassay for %%%PDGF%%% was developed with a sensitivity of congruent to 0.2 ng/ml. Levels of %%%PDGF%%% in plasma/serum were measured and compared with %%%PDGF%%% levels determined by a receptor-competition assay and by a standard biological assay measuring incorporation of [3H]thymidine into 3T3 cells. Radioimmunoassay showed apparent %%%PDGF%%% levels of 50 ng/ml in human plasma and 103 ng/ml in serum. The 50 ng/ml %%%PDGF%%% in plasma was unexpected because the plasma samples contained little or no platelet release products as determined by very low levels of platelet factor 4. We therefore sought an immunologically reactive %%%PDGF%%% molecule in hum

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DIALOG(R)File 155:MEDLINE(R)

(c) format only 1997 Knight-Ridder Info. All rts. reserv.an plasma. No immunolog was detected by immunodiffusion an

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Stimulation of growth of human breast cancer cells (T4 derived growth factor [published erratum appears in Cancer Lett 1991 9/3,AB/3
DIALOG(R)File 155:MEDLINE(R)
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07050111 91266260
Stimulation of growth of human breast cancer cells (T47D) by platelet derived growth factor [published erratum appears in Cancer Lett 1991 Sep;59(3):267]
Ginsburg E; Vonderhaar BK7D) by platelet%%%alysis or when plasma was treated w immunoaffinity gel. Subsequently, a 125I-%%%PDGF%%%-binding protein was identified; the 125I-%%%PDGF%%% -plasma-binding protein complex was not reactive with %%%anti%%%-%%%PDGF%%% immunoglobulin. Correction for 125I-%%%PDGF%%% bound by the plasma-binding protein established serum levels of %%%PDGF%%% of congruent to 50 ng/ml; congruent to 50 ng/ml %%%PDGF%%% was found in serum by radioreceptor-competition assays and by mitogenic assays as well. The plasma-binding protein may serve to clear %%%PDGF%%% released in the circulation, thereby limiting %%%PDGF%%% activity to its local interactions at the site of blood-vessel injury.
? ds

Set	Items	Description
S1	115	PDGF AND (ANTIBODIES OR ANTIBODY) AND CELL()PROLIF?
S2	73	S1 AND PY>1991
S3	42	S1 NOT S2
S4	28	S3 NOT PY=1991
S5	14	S3 AND PY=1991
S6	683	PDGF AND (ANTIBODIES OR ANTIBODY) NOT S1
S7	431	S6 AND PY>1991
S8	252	S6 NOT S7
S9	40	S8 AND ANTI()PDGF

? logout

19sep97 08:41:05 User217743 Session D414.3
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$0.00 42 Type(s) in Format 6
$3.00 60 Type(s) in Format 95 (KWIC)
$1.80 9 Type(s) in Format 4 (UDF)
$4.80 111 Types
$17.28 Estimated cost File155
$17.28 Estimated cost this search
$17.28 Estimated total session cost 0.424 Hrs.
Logoff: level 97.08.03 D 08:41:05